targeting of anti-tumo[redacted]gents.

=> d his

(FILE 'USPAT' ENTERED AT 09:07:26 ON 10 NOV 1997)

L1 70 S ZINC(W)FINGERS

L2 3 S ZIF268

08/793 408
AH # 9

13548838 BIOSIS Number: 99548838
Phage display of RNA binding **zinc fingers** from transcription factor IIIA
Friesen W J; Darby M K
Dep. Microbiol. Immunol., Kimmel Cancer Inst., Thomas Jefferson Univ., 233 S. 10th St., Philadelphia, PA 19107, USA
Journal of Biological Chemistry 272 (17). 1997. 10994-10997.
Full Journal Title: Journal of Biological Chemistry
ISSN: 0021-9258
Language: ENGLISH
Print Number: Biological Abstracts Vol. 103 Iss. 012 Ref. 172266
QP501.J7

Zinc fingers in transcription factor IIIA (TFIIIA) contribute differentially to RNA and DNA binding affinity. We investigated whether the same putative alpha-helix amino acids in TFIIIA **zinc fingers** are essential for both RNA and DNA binding. In published structures, **zinc fingers** make DNA base contacts through amino acids -1, +2, +3, and +6 of the recognition helix. Alanine **substitution** at these four positions were made in TFIIIA RNA binding **zinc fingers**, tz4-7 and DNA binding **zinc fingers**, tz1-3. **Substitution** in **zinc fingers** 4 or 6 of tz4-7 reduced RNA affinity 77- and 38-fold, respectively, whereas **substitution** in **zinc fingers** 5 or 7 had little effect. DNA binding affinity of tz1-3 was eliminated by alanine **substitution** in any one zinc finger. We determined which amino acids supported RNA binding by phage display of a **library** of zinc finger 4 mutants. Lysine at helix position -1 of zinc finger 4 was conserved in all selected tz4-7 fusions. Point **mutation** of Lys-1 to alanine in zinc finger 4 reduced tz4-7 RNA affinity 30-fold. We propose that RNA binding by TFIIIA shows similarity to DNA binding in the use of the recognition helix. Helix positions -1 and +2 may have particular

13312450 BIOSIS Number: 99312450
A zinc finger directory for high-affinity DNA recognition
Jamieson A C; Wang H; Kim S-H
Sangamo Biosci., 9125 E. 10th Drive, Aurora, CO 80010, USA
Proceedings of the National Academy of Sciences of the United States of America 93 (23). 1996. 12834-12839.
Full Journal Title: Proceedings of the National Academy of Sciences of the United States of America
ISSN: 0027-8424
Language: ENGLISH
Print Number: Biological Abstracts Vol. 103 Iss. 002 Ref. 015564

We have used two monovalent phage display **libraries** containing variants of the Zif268 DNA-binding domain to obtain families of **zinc fingers** that bind to alterations in the last 4 hp of the DNA sequence of the Zif268 consensus operator, GCG TGGGCG. Affinity selection was performed by altering the Zif268 operator three base pairs at a time, and simultaneously selecting for sets of 16 related DNA sequences. In this way, only four experiments were required to select for all possible 64 combinations of DNA triplet sequences. The results show that (i) for high-affinity DNA binding in the range observed for the Zif268 wild-type complex (K-d = 0.5-5 nM), finger 1 specifically requires the arginine at the carboxy terminus of its recognition helix that forms a bidentate hydrogen-bond with the guanine base (G) in the crystal structure of Zif268 complexed to its DNA operator sequence GCG TGG GCG; (ii) when the guanine base (G) is **replaced** by A, C, or T, a lower-affinity family (K-d gtoreq 50 nM) can be detected that shows an overall tendency to bind G-rich DNA; (iii) the residues at position 2 on the finger 2 recognition helix do not appear to interact strongly with the complementary 5' base in the

finger 1 binding site; and (iv) unexpected **substitution** at the amino terminus of finger 1 [redacted] occasionally result in specificity for the 3' base in the finger 1 binding site. A DNA recognition directory was constructed for high-affinity **zinc fingers** that recognize all three bases in a DNA triplet for seven sequences of the type GNN. Similar approaches may be applied to other **zinc fingers** to broaden the scope of the directory.

11662536 BIOSIS Number: 98262536

A conformationally homogeneous combinatorial peptide **library**

Bianchi E; Folgori A; Wallace A; Nicotra M; Acali S; Phalipon A; Barbato G; Bazzo R; Cortese R; Felici F; Pessi A

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Journal of Molecular Biology 247 (2). 1995. 154-160.

Full Journal Title: Journal of Molecular Biology

ISSN: 0022-2836

Language: ENGLISH

Print Number: Biological Abstracts Vol. 099 Iss. 012 Ref. 167454

In search for a rational way to convert the information encoded in peptide structures into peptidomimetics, major progress could be made by coupling the power of selection methods, now enormously increased in number as a result of the development of combinatorial peptide **libraries**, with the rational design of structure-inducing templates for the selectable sequences. The availability of **libraries** of peptides with predetermined structure would enable selection-driven peptidomimetic design, whereby a conformational model for the peptide pharmacophore would be directly derived from the screening, allowing the design of a suitable non-peptidic scaffold to **replace** the peptide backbone. We describe here the first example of a conformationally homogeneous combinatorial peptide **library** , which yields ligands with the expected structure upon selection. The **library** was built by randomising five positions in the alpha-helical portion of a 26 amino acid Cys-2His-2 consensus "zinc-finger" motif. Since in **zinc-fingers** metal coordination and folding are coupled, in our **library** metal-dependent binding represents a built-in control against the selection of structurally undefined sequences. The alpha-helical **library** was produced as both fusion with the pVIII protein of filamentous phage and soluble peptides by chemical synthesis, the latter enabling the expansion of the selectable repertoire by the inclusion of non-coded amino acids. The two **libraries** were independently screened with the same receptor (a monoclonal IgA reactive against the lipopolysaccharide of the human pathogen Shigella flexneri), yielding a very similar consensus. In particular, the peptides defined by both methods showed very strong, zinc-dependent binding to the IgA. The geometrical arrangement of the side-chains of the selected peptide pharmacophore was shown by circular dichroism, Co(II)-complex absorption and high-resolution NMR to be structurally invariant with respect to the parent zinc-finger.

11112516 BIOSIS Number: 97312516

In vitro selection of **zinc fingers** with altered DNA-binding specificity

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Biochemistry 33 (19). 1994. 5689-5695.

Full Journal Title: Biochemistry

ISSN: 0006-2960

Language: ENGLISH

Print Number: Biological Abstracts Vol. 098 Iss. 002 Ref. 019028

We have used random mutagenesis and phage display to alter the DNA-binding specificity of Zif268, a transcription factor that contains three zinc finger domains. Four residues in the helix of finger 1 of Zif268

that potentially mediate DNA binding were identified from an X-ray structure of the Zif268-DNA complex. A **library** was constructed in which these residues were randomly **mutated** and the Zif268 variants were fused to a truncated version of the gene III coat protein on the surface of M13 filamentous phage particles. The phage displayed the mutant proteins in a monovalent fashion and were sorted by repeated binding and elution from affinity matrices containing different DNA sequences, When the matrix contained the natural nine base pair operator sequence 5'-GCG-TGG-GCG-3', native-like **zinc fingers** were isolated. New finger 1 variants were found by sorting with two different operators in which the singly modified triplets, GTG and TCG, **replaced** the native finger 1 triplet, GCG. Overall, the selected finger 1 variants contained a preponderance of polar residues at the four sites. Interestingly, the net charge of the four residues in any selected finger never deviated more that one unit from neutrality despite the fact that about half the variants contained three or four charged residues over the four sites. Measurements of the dissociation constants for two of these purified finger 1 variants by gel-shift assay showed their specificities to vary over a 10-fold range, with the greatest affinity being for the DNA binding site for which they were sorted. We were unable to enrich for clones that bind to five other binding sites (ACG, CCG, CGC, ATA, and TAT), suggesting modification of just these four residues in finger I may not allow it to adapt to all DNA binding sites. The studies show it is possible to isolate **zinc fingers** by phage display that distinguish operator sequences that differ by a single base change. Moreover, such selection methods should aid in clarifying rules for zinc finger-DNA recognition.

8616938 EMBASE No: 92293814

Cloning of GT box-binding proteins: A novel Sp1 multigene family regulating T-cell receptor gene expression

Kingsley C.; Winoto A.

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MOL. CELL. BIOL. (USA) , 1992, 12/10 (4251-4261) CODEN: MCEBD ISSN: 0270-7306

LANGUAGES: English SUMMARY LANGUAGES: English

Analysis of a T-cell antigen receptor (TCR) alpha promoter from a variable gene segment (V) revealed a critical GT box element which is also found in upstream regions of several Valpha genes, TCR enhancer, and regulatory elements of other genes. This element is necessary for TCR gene expression and binds several proteins. These GT box-binding proteins were identified as members of a novel Sp1 multigene family. Two of them, which we term Sp2 and Sp3, were cloned. Sp2 and Sp3 contain **zinc fingers** and transactivation domains similar to those of Sp1. Like Sp1, Sp2 and Sp3 are expressed ubiquitously, and their in vitro-translated products bind to the GT box in TCR Valpha promoters. Sp3, in particular, also binds to the Sp1 consensus sequence GC box and has binding activity similar to that of Sp1. As the GT box has also previously been shown to play a role in gene regulation of other genes, these newly isolated Sp2 and Sp3 proteins might regulate expression not only of the TCR gene but of

09142176 97296423

A target of phosphatidylinositol 3,4,5-trisphosphate with a zinc finger motif similar to that of the ADP-ribosylation-factor GTPase-activating protein and two pleckstrin homology domains.

Tanaka K; Imajoh-Ohmi S; Sawada T; Shirai R; Hashimoto Y; Iwasaki S; Kaibuchi K; Kanaho Y; Shirai T; Terada Y; Kimura K; Nagata S; Fukui Y

Department of Applied Biological Chemistry, The Graduate School of Agriculture and Life Sciences, University of Tokyo, Bunkyo-ku, Japan.

Eur J Biochem (GERMANY) Apr 15 1997, 245 (2) p512-9, ISSN 0014-2956 Journal Code: EMZ

Languages: ENGLISH

Document type: JOURNAL ARTICLE

We have purified a protein that binds phosphatidylinositol

3,4,5-trisphosphate [PtdIns(3,4,5)P3] using beads bearing a PtdIns(3,4,5)P3 analogue. This protein, with a molecular mass of 43 kDa, was termed PtdIns(3,4,5)P3-binding protein. The partial amino acid sequences were determined and a full-length cDNA encoding the protein was isolated from bovine brain cDNA **library**. The clone harbored an open reading frame of 373 amino acids which contained one zinc finger motif similar to that of ADP-ribosylation-factor GTPase-activating protein and two pleckstrin homology domains. The entire sequence was 83% similar to centaurin alpha, another PtdIns(3,4,5)P3-binding protein. The protein bound PtdIns(3,4,5)P3 with a higher affinity than it did inositol 1,3,4,5-tetrakisphosphate, phosphatidylinositol 4,5-bisphosphate, phosphatidylinositol 3,4-bisphosphate, and phosphatidylinositol 3-phosphate suggesting that the binding to PtdIns(3,4,5)P3 was specific. The binding activity was weaker in the mutants with a point **mutation** in the conserved sequences in each pleckstrin homology domain. Introduction of both **mutations** abolished the activity. These results suggest that this new binding protein binds PtdIns(3,4,5)P3 through two pleckstrin domains present in the molecule.

08759089 96032831

A novel DNA-binding domain that may form a single zinc finger motif.

Yanagisawa S

Department of Life Sciences (Chemistry), Graduate School of Arts and Sciences, University of Tokyo, Japan.

Nucleic Acids Res (ENGLAND) Sep 11 1995, 23 (17) p3403-10, ISSN 0305-1048 Journal Code: O8L

Languages: ENGLISH

Document type: JOURNAL ARTICLE

MNB1a is a DNA-binding protein from maize that interacts with the 35S promoter of cauliflower mosaic virus. This protein did not show significant homologies with any other DNA-binding protein and MNB1a seemed to be a member of a multigene family. In this study, isolation of cDNAs from the gene family to which MNB1a belongs revealed a unique conserved domain, referred to herein as the Dof domain, that contains a novel cysteine-rich motif for a single putative zinc finger. The amino acid sequence of the Dof domain and the arrangement of cysteine residues in this domain differ from those of known zinc finger motifs. However, the Dof domain was shown to be a DNA-binding domain that required Zn2+ ions for activity. **Mutations** at cysteine residues eliminated the DNA-binding activity of MNB1a. Thus, the Dof domain may be classified as a novel zinc finger motif. In addition, Southern blot analysis and a survey of DNA databases suggested that proteins that include Dof domains might exist in other eukaryotes, at least

08728242 94119100

The Drosophila l(2)35Ba/nocA gene encodes a putative Zn finger protein involved in the development of the embryonic brain and the adult ocellar structures.

Cheah PY; Meng YB; Yang X; Kimbrell D; Ashburner M; Chia W

Drosophila Neurobiology Laboratory, National University of Singapore.

Mol Cell Biol (UNITED STATES) Feb 1994, 14 (2) p1487-99, ISSN 0270-7306 Journal Code: NGY

Languages: ENGLISH

Document type: JOURNAL ARTICLE

The Drosophila l(2)35Ba/nocA gene is involved in the development of the adult ocelli and the embryonic head. **Mutations** in this gene lead to at least two distinct phenotypes. Several larva lethal l(2)35Ba alleles cause both hypertrophy and mislocation of the embryonic supraesophageal ganglion (brain) to the dorsal surface of the embryo. A second class of mutant alleles (nocA) is homozygous viable, but the surviving adults either lack or have greatly reduced ocelli and associated bristles. The l(2)35Ba/nocA gene encodes an approximately 3.0-kb transcript doublet; all l(2)35Ba alleles which have been physically mapped delete or disrupt the transcribed region, whereas all of the viable nocA alleles are caused by gross chromosomal aberrations with breakpoints near the 3'-flanking region of the gene. Several nocA breakpoint alleles downregulate the level of

l(2)35Ba/nocA transcripts in adults, and their defective ocellar phenotype also fails to be complemented by the lethal alleles, indicating that l(2)35Ba and nocA are different phenotypic manifestations of **mutations** in the same gene. In the l(2)35Ba mutant embryos, cells from the procephalic lobe which normally migrate over and overlie the supraesophageal ganglion during head involution can become incorporated into the supraesophageal ganglion; many of these misplaced cells, which normally form the frontal sac, also adopt a neuronal fate. Sequence analysis of two full-length l(2)35Ba/nocA cDNAs with distinct polyadenylation sites shows that they encode the same deduced protein of 537 amino acids with a serine- and threonine-rich N-terminal region, two putative zinc finger motifs near the carboxyl terminus, and several alanine-rich domains. Consistent with the observed embryonic phenotype, l(2)35Ba/nocA shows a complex embryonic expression pattern which includes the procephalic lobe.

08702863 96397632
Computational screening of combinatorial **libraries**.
Zheng Q; Kyle DJ
Scios Nova, Inc., Sunnyvale, CA 94086, USA.
Bioorg Med Chem (ENGLAND) May 1996, 4 (5) p631-8, ISSN 0968-0896
Journal Code: B38
QP501.B57 (Adams)
Languages: ENGLISH
Document type: JOURNAL ARTICLE
order
We first review existing computational methods with an intrinsic combinatorial feature, then describe a new computational method for screening combinatorial **libraries** using a recently developed multicopy sampling technique. The new method differs from the existing ones in that it can be used to screen simultaneously an entire **library** of molecules, instead of the individual molecules in a **library**. As an example, we have applied the method to study site-directed amino acid **substitutions** in a protein. After two rounds of **library** screening, we identified the energetically most stable **substitutions** along with their optimal conformations from all natural amino acids. In principle, the method is generally applicable to study ligand-host systems.

08503105 96081683
[Negative repressor THZif-1 of protooncogene c-myc]
Yokoyama K; Tsutsui H; Fujita A
RIKEN (The Institute of Physical and Chemical Research), Tsukuba Life Science Center.
Nippon Rinsho (JAPAN) Nov 1995, 53 (11) p2827-36, ISSN 0047-1852
Journal Code: KIM
Languages: JAPANESE Summary Languages: ENGLISH
Document type: JOURNAL ARTICLE; REVIEW; REVIEW, TUTORIAL English Abstract
A human recombinant cDNA clone that encoded 253 amino acids residues of a zinc-finger protein (THZif-1) was cloned by screening a cDNA **library** prepared from human promyelocytic leukemia HL60 cells with synthetic oligodeoxynucleotide probes that corresponded to the amino acid sequences of tryptic peptides derived from the DNA-binding protein specific for the nuclease-hypersensitive element (NHE) of the human c-myc gene. The predicted amino acid sequence of THZif-1 included a DNA-binding domain that contained five tandemly repeated zinc finger motifs. The three amino-terminal sets of zinc finger motifs, including the second finger, were found to be responsible for high-affinity interactions with the triple-helical conformation of NHE, as well as for high-affinity binding to the single-pyrimidine-rich strand of NHE in a sequence-specific manner. Cotransfection, trans-activation and in vitro transcription studies using the wild-type form and THZif-1 with a **mutated** second zinc finger motif demonstrated that the DNA-binding activity specific for H-form DNA of NHE was a prerequisite for the negative regulation of the expression of the

08351505 95379762

The Aspergillus uvsH gene encodes a product homologous to yeast RAD18 and Neurospora UVS-2.

Yoon JH; Lee BJ; Kang HS

Department of Microbiology, Seoul National University, Korea.

Mol Gen Genet (GERMANY) Jul 28 1995, 248 (2) p174-81, ISSN 0026-8925 Journal Code: NGP

Languages: ENGLISH

Document type: JOURNAL ARTICLE

The uvsH DNA repair gene of Aspergillus nidulans has been cloned by complementation of the uvsH77 **mutation** with a cosmid **library** containing genomic DNA inserts from a wild-type strain. Methylmethane sulfonate (MMS)-resistant transformants were obtained on medium containing 0.01% MMS, to which uvsH mutants exhibit high sensitivity. Retransformation of uvsH77 mutants with the rescued cosmids from the MMS-resistant transformants resulted in restoration of both UV and MMS resistance to wild-type levels. Nucleotide sequence analysis of the genomic DNA and cDNA of the uvsH gene shows that it has an open reading frame (ORF) of 1329 bp, interrupted by two introns of 51 and 61 bp. A 2.4 kb transcript of the uvsH gene was detected by Northern blot analysis. Primer extension analysis revealed that transcription starts at 31 bp upstream from the translation initiation codon. This gene encodes a predicted polypeptide of 443 amino acids, which has two unique zinc finger motifs. The proposed polypeptide displays 39% identity to the Neurospora crassa UVS-2 protein and 24% identity to the Saccharomyces cerevisiae RAD18 protein. The sequence similarity is particularly high in three domains. One zinc finger (RING finger) motif is located in the first domain close to the N-terminus. The other zinc finger motif is in the second domain. In the third domain, the **mutation** sites in both the uvsH77 and uvsH304 alleles were identified.(ABSTRACT TRUNCATED AT 250 WORDS)

7/3,AB/24 (Item 17 from file: 155)

DIALOG(R)File 155:MEDLINE(R)

08305132 95325643

Surface plasmon resonance based kinetic studies of zinc finger-DNA interactions.

Yang WP; Wu H; Barbas CF 3rd

Department of Molecular Biology, Scripps Research Institute, La Jolla, CA 92037, USA.

J Immunol Methods (NETHERLANDS) Jun 14 1995, 183 (1) p175-82, ISSN 0022-1759 Journal Code: IFE

QR183 . J6

Languages: ENGLISH

Document type: JOURNAL ARTICLE

Libraries of the zinc finger DNA binding protein, Zif268, have been constructed and selected for affinity and specificity toward DNA targets using the phage display technique (Wu et al., 1995). Mutant proteins were purified to homogeneity and were characterized for their ability to interact with their DNA targets using a real-time biomolecular interaction assay (BIA). One mutant protein, C7, bound the Zif268 consensus binding sequence with a 13-fold increase in affinity as compared to the wild-type Zif268 protein. Mutant proteins with moderate affinity for new DNA targets within a consensus sequence of HIV-1 have also been obtained. Surface plasmon resonance based BIA has provided invaluable kinetic information which offers insights into the mechanism of protein-DNA interactions.

8298410 95318055

Identification and functional characterization of an erythroid-specific enhancer in the L-type pyruvate kinase gene.

Lacronique V; Lopez S; Miquerol L; Porteu A; Kahn A; Raymondjean M

Institut Cochin de Genetique Moleculaire, Unite 129 INSERM, Universite Rene Descartes, Paris, France.

J Biol Chem (UNITED STATES) Jun 23 1995, 270 (25) p14989-97, ISSN 0021-9258 Journal Code: HIV

Languages: ENGLISH

Document type: JOURNAL ARTICLE

The rat L-type pyruvate kinase gene is transcribed either from promoter L in the liver or promoter L' in erythroid cells. We have now cloned and functionally characterized an erythroid-specific enhancer, mapped in the fetal liver as hypersensitive site B (HSSB) at 3.7 kilobases upstream from the promoter L'. Protein-DNA interactions were examined in the 200-base pair core of the site by in vivo footprinting experiments. In the fetal liver, footprints were revealed at multiple GATA and CACC/GT motifs, whose association is the hallmark of erythroid-specific regulatory sequences. Functional analysis of the HSSB element in transgenic mice revealed properties of a cell-restricted enhancer. Indeed, this element was able to activate the linked ubiquitous herpes simplex virus thymidine kinase promoter in erythroid tissues. The activation was also observed in a variety of nonerythroid tissues known to synthesize GATA-binding factors. In the context of L'-PK transgenes, HSSB was not needed for an erythroid-specific activation of the L' promoter, while it was required to stimulate the L' promoter activity to a proper level. Finally, HSSB cannot be **replaced** by strong ubiquitous viral or cellular enhancers, suggesting a preferential interaction of the HSSB region with the L' promoter.

08082052 95066376

A new nuclear suppressor system for a mitochondrial RNA polymerase mutant identifies an unusual zinc-finger protein and a polyglutamine domain protein in Saccharomyces cerevisiae.

Brohl S; Lisowsky T; Riemen G; Michaelis G

Botanisches Institut, Universitat Dusseldorf, Germany.

Yeast (ENGLAND) Jun 1994, 10 (6) p719-31, ISSN 0749-503X

Journal Code: YEA

Languages: ENGLISH

Document type: JOURNAL ARTICLE

A yeast strain with a point **mutation** in the nuclear gene for the core subunit of mitochondrial RNA polymerase was used to isolate new extragenic suppressors. Spontaneously occurring phenotypical revertants were analysed by crosses with the wild-type and tetrad dissection. One of the new nuclear suppressor mutants was characterized by temperature-sensitive growth on non-fermentable carbon sources. This mutant was transformed with a genomic yeast **library**. Two independent types of DNA clones were isolated which both complemented the temperature-sensitive defect. Subcloning and DNA sequencing identified two novel yeast genes which code for proteins with the characteristic features of transcription factors. Both factors exhibit highly structured protein domains consisting of runs and clusters of asparagine and glutamine residues. One of the proteins contains in addition zinc-finger domains of the C2H2-type. Therefore the genes are proposed to be named AZF1 (asparagine-rich zinc-finger protein) and PGD1 (polyglutamine domain protein). Gene disruption of both reading frames has no detectable influence on the vegetative growth on complete glucose or glycerol media, indicating that the genes may act as high copy number suppressors of the mutant defect. Additional transformation experiments showed that AZF1 is also an efficient suppressor for the original defect in the core subunit of

07883404 94185017

The ETO portion of acute myeloid leukemia t(8;21) fusion transcript encodes a highly evolutionarily conserved, putative transcription factor.

Erickson PF; Robinson M; Owens G; Drabkin HA

Division of Medical Oncology, University of Colorado Health Sciences and Cancer Center, Denver 80262.

Cancer Res (UNITED STATES) Apr 1 1994, 54 (7) p1782-6, ISSN 0008-5472

Journal Code: CNF

Contract/Grant No.: P01-HD017449, HD, NICHD

Languages: ENGLISH

Document type: JOURNAL ARTICLE

The 8;21 translocation, t(8;21)(q22;q22.3), is seen only in acute myelogenous leukemia and is characteristically associated with the M2

subtype. Subsequent to our identification of the t(8;21) breakpoint region on chromosome 21, we reported that the translocation results in the fusion of the AML1 gene on chromosome 21 with a novel gene on chromosome 8 which we called ETO (for eight twenty-one). Recently, the AML1 portion of the fusion protein has been shown to correspond to the DNA-binding and dimerization domains of the mouse gene, polyoma enhancer binding protein 2 alpha B (pebp 2 alpha B). We report here the complete sequence of the ETO portion of the fusion transcript as compiled from complementary DNAs from a t(8;21) AML patient and compare this with the ETO sequence from a mouse brain transcript. The deduced amino acid sequences are 99% identical. ETO has several features consistent with it being a transcription factor. The ETO sequence is different from the portion of PEBP 2 alpha B it **replaces** in the AML1/ETO fusion protein, except for their common high content of proline, serine, and threonine residues. Because neither the putative **zinc fingers** nor the TAF110 homology domain of ETO is present in PEBP2 alpha B, one might expect functional differences in the ability of AML1/ETO protein to affect the levels of transcription of genes normally regulated to some degree by AML1 (PEBP2 alpha B) during myeloid differentiation. The relatively high levels of ETO in developing brain suggest that it could be involved in the regulation of some aspect of neural proliferation or differentiation.

7/3,AB/29 (Item 22 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

07793670 93241158

The Neurospora uvs-2 gene encodes a protein which has homology to yeast RAD18, with unique zinc finger motifs [published erratum appears in Mol Gen Genet 1994 Mar;242(6):743]

Tomita H; Soshi T; Inoue H

Department of Regulation Biology, Faculty of Science, Saitama University, Urawa, Japan.

Mol Gen Genet (GERMANY) Apr 1993, 238 (1-2) p225-33, ISSN 0026-8925 Journal Code: NGP

Languages: ENGLISH

Document type: JOURNAL ARTICLE

A clone containing the DNA repair gene uvs-2 of Neurospora crassa was identified from a Neurospora genomic DNA **library** using the sib-selection method. Transformants were screened for resistance to methyl methane sulfonate (MMS). A DNA fragment that complements the uvs-2 **mutation** was subcloned by monitoring its ability to transform the uvs-2 mutant to MMS resistance. Deletion analysis of the cloned DNA indicated that the size of the uvs-2 gene is approximately 1.6 kb. The identity of the uvs-2 gene was verified by restriction fragment length polymorphism (RFLP) mapping. The sensitivity of the transformant to three different mutagens was similar to that of the wild-type strain. Nucleotide sequences of genomic DNA and cDNA of the uvs-2 gene indicated that it has an open reading frame (ORF) of 1572 bp with a 69 bp intron in the middle of the sequence. Two transcription initiation sites located around 73 bp and 290 bp upstream of the translation initiation codon were identified by primer extension experiments. Northern analysis revealed that the nature transcript of the uvs-2 gene was about 1.8 kb long. The uvs-2 gene ORF is deduced to encode a polypeptide of 501 amino acids with a molecular mass of 54 kDa. The proposed polypeptide has 25% identity to the RAD18 polypeptide of Saccharomyces cerevisiae and contains two unique zinc finger motifs for nucleic acid binding. Similarities between the phenotypes of the rad18 and uvs-2 mutants suggest that the uvs-2 gene encodes a protein which is involved in postreplication repair, rather than excision repair.

7/3,AB/30 (Item 23 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

07682063 94040730

Perinatal lethali[redacted] and defects in hindbrain [redacted]elopment in mice homozygous for a targeted **mutation** of the zinc finger gene Krox20.

Swiatek PJ; Gridley T

Roche Institute of Molecular Biology, Roche Research Center, Nutley, New Jersey 07110.

Genes Dev (UNITED STATES) Nov 1993, 7 (11) p2071-84, ISSN 0890-9369 Journal Code: FN3

QH426.G46

Languages: ENGLISH

Document type: JOURNAL ARTICLE

Krox20 is a zinc finger gene expressed in rhombomeres 3 and 5 during hindbrain development in vertebrates. Mice homozygous for a targeted **mutation** that deletes the majority of the Krox20 genes, including the zinc finger DNA-binding domain, died shortly after birth. The primary phenotype of the homozygous mutant animals was the loss of rhombomeres 3 and 5. This resulted in fusions of the trigeminal ganglion with the facial and vestibular ganglia, and of the superior ganglia of the glossopharyngeal and vagus nerves. These fusions resulted in a disorganization of the nerve roots of these ganglia as they entered the brain stem. These data demonstrate that Krox20 plays an essential role during development of the hindbrain and associated cranial sensory ganglia in mice.

07291220 93087555

Pur-1, a zinc-finger protein that binds to purine-rich sequences, transactivates an insulin promoter in heterologous cells.

Kennedy GC; Rutter WJ

Hormone Research Institute, University of California, San Francisco 94143-0534.

Proc Natl Acad Sci U S A (UNITED STATES) Dec 1 1992, 89 (23) p11498-502, ISSN 0027-8424 Journal Code: PV3

Contract/Grant No.: DK08132, DK, NIDDK; DK21344, DK, NIDDK

Languages: ENGLISH

Document type: JOURNAL ARTICLE

Purine-rich stretches of nucleotides (GAGA boxes) are often found just upstream of transcription start sites in many genes, including insulin. **Mutational** analysis suggests that the GAGA box plays an important role in transcription of the rat insulin I gene. We identify here at least four different proteins that bind specifically to the insulin GAGA box. Using a GAGA oligonucleotide, we have isolated a cDNA encoding a sequence-specific protein from a HIT (hamster insulinoma cell line) lambda gt11 **library** . This protein, which we designate Pur-1 (for purine binding), binds to the GAGA boxes of the rat insulin I and II genes and the human islet amyloid polypeptide gene. Pur-1 is a potent transactivator in both pancreatic and nonpancreatic cells. Furthermore, Pur-1 is able to activate an intact insulin promoter in HeLa cells, where it is normally

07112267 92236619

Expression cloning of a novel zinc finger protein that binds to the c-fos serum response element.

Attar RM; Gilman MZ

Cold Spring Harbor Laboratory, New York 11724.

Mol Cell Biol (UNITED STATES) May 1992, 12 (5) p2432-43, ISSN 0270-7306 Journal Code: NGY

Contract/Grant No.: CA45642, CA, NCI; CA46370, CA, NCI

QH506.M6

Languages: ENGLISH

Document type: JOURNAL ARTICLE

Induction of c-fos transcription by serum growth factors requires the serum response element (SRE). The SRE is a multifunctional element which responds to several positively and negatively acting signals. To identify cellular proteins that might mediate functions of the SRE, we screened a human cDNA expression **library** with an SRE probe. We report the isolation and characterization of SRE-ZBP, a previously unidentified SRE-binding protein. SRE-ZBP is a member of the C2H2 zinc finger family of proteins exemplified by TFIIIA and the Drosophila Kruppel protein. The

seven tandemly repeated zinc finger motifs in SRE-ZBP are sufficient for high-affinity binding to the SRE. We show that SRE-ZBP is a nuclear protein and identify a candidate cellular protein encoded by the SRE-ZBP gene. Because we cannot detect any DNA-binding activity attributable to the endogenous protein, we propose that SRE-ZBP activity may be subject to posttranslational regulation. Like c-fos mRNA, SRE-ZBP mRNA is serum inducible in HeLa cells, but with slower kinetics. The role of SRE-ZBP in the regulation of c-fos transcription remains unestablished, but this protein binds to a region of the SRE where **mutations** lead to derepression.

185108 DBA Accession No.: 95-11929 PATENT

New zinc finger-nucleotide binding polypeptides - gene cloning, expression, protein engineering and phage display, for use as an antitumor or virucide agent, or in treating plants

AUTHOR: Barbas III C F; Gottesfeld J M; Wright P E

PATENT ASSIGNEE: Scripps-Res.Inst. 1995

PATENT NUMBER: WO 9519431 PATENT DATE: 950720 WPI ACCESSION NO.: 95-263862 (9534)

PRIORITY APPLIC. NO.: US 312604 APPLIC. DATE: 940928

NATIONAL APPLIC. NO.: WO 95US829 APPLIC. DATE: 950118

LANGUAGE: English

ABSTRACT: A new zinc finger-nucleotide binding protein (ZFNB) variant has at least 2 zinc finger modules that bind to a cellular DNA or RNA (e.g. an onco-promoter, virus promoter, HTLV-1 virus, HTLV-2 virus, HIV virus-1, HIV virus-2 sequence or oncogene) and modulate its function. A ZFNB protein variant may be isolated by: identifying amino acids binding to and modulating function of a 1st sequence; creating a phage display peptide **library** by polymerase chain reaction randomized **substitution** ; expressing in a host; and isolating a clone producing a variant modulating function of a 2nd sequence. A ZFNB protein gene may be tested by linking to a 1st inducible promoter in a vector with a beta-galactosidase (EC-3.2.1.23) reporter gene operably linked to a 2nd inducible promoter and a ZFNB motif, under interaction conditions, and measuring the effect of the ZFNB protein on reporter gene expression. The protein may be zif260 or TFIIIA, with a TGEKP linker between **zinc fingers**. The ZFNB protein may be used e.g. in therapy of cancer and virus-induced cell proliferative

13548838 BIOSIS Number: 99548838

Phage display of RNA binding **zinc fingers** from transcription factor IIIA

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Journal of Biological Chemistry 272 (17). 1997. 10994-10997.

Full Journal Title: Journal of Biological Chemistry

ISSN: 0021-9258

Language: ENGLISH

Print Number: Biological Abstracts Vol. 103 Iss. 012 Ref. 172266

Zinc fingers in transcription factor IIIA (TFIIIA) contribute differentially to RNA and DNA binding affinity. We investigated whether the same putative alpha-helix amino acids in TFIIIA **zinc fingers** are essential for both RNA and DNA binding. In published structures, **zinc fingers** make DNA base contacts through amino acids -1, +2, +3, and +6 of the recognition helix. Alanine **substitution** at these four positions were made in TFIIIA RNA binding **zinc fingers**, tz4-7 and DNA binding **zinc fingers**, tz1-3. **Substitution** in **zinc fingers** 4 or 6 of tz4-7 reduced RNA affinity 77- and 38-fold, respectively, whereas **substitution** in **zinc fingers** 5 or 7 had little effect. DNA binding affinity of tz1-3 was eliminated by alanine **substitution** in any one zinc finger. We determined which amino acids supported RNA binding by phage display of a **library** of zinc finger 4 mutants. Lysine at helix position -1 of zinc finger 4 was conserved in all selected tz4-7 fusions. Point **mutation** of Lys-1 to alanine in zinc finger 4 reduced tz4-7 RNA affinity 30-fold. We propose that RNA binding by TFIIIA shows similarity to DNA binding in the use of the recognition helix. Helix positions -1 and +2 may have particular

13312450 BIOSIS Number: 99312450

A zinc finger directory for high-affinity DNA recognition

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Sangamo Biosci., 9125 E. 10th Drive, Aurora, CO 80010, USA

Proceedings of the National Academy of Sciences of the United States of America 93 (23). 1996. 12834-12839.

Full Journal Title: Proceedings of the National Academy of Sciences of the United States of America

ISSN: 0027-8424

Language: ENGLISH

Print Number: Biological Abstracts Vol. 103 Iss. 002 Ref. 015564

We have used two monovalent phage display **libraries** containing variants of the Zif268 DNA-binding domain to obtain families of **zinc fingers** that bind to alterations in the last 4 hp of the DNA sequence of the Zif268 consensus operator, GCG TGGGCG. Affinity selection was performed by altering the Zif268 operator three base pairs at a time, and simultaneously selecting for sets of 16 related DNA sequences. In this way, only four experiments were required to select for all possible 64 combinations of DNA triplet sequences. The results show that (i) for high-affinity DNA binding in the range observed for the Zif268 wild-type complex (K-d = 0.5-5 nM), finger 1 specifically requires the arginine at the carboxy terminus of its recognition helix that forms a bidentate hydrogen-bond with the guanine base (G) in the crystal structure of Zif268 complexed to its DNA operator sequence GCG TGG GCG; (ii) when the guanine base (G) is **replaced** by A, C, or T, a lower-affinity family (K-d gtoreq 50 nM) can be detected that shows an overall tendency to bind G-rich DNA; (iii) the residues at position 2 on the finger 2 recognition helix do not appear to interact strongly with the complementary 5' base in the

finger 1 binding site; and (iv) unexpected **substitutions** at the amino terminus of finger 1 occasionally result in specificity for the 3' base in the finger 1 binding site. A DNA recognition directory was constructed for high-affinity **zinc fingers** that recognize all three bases in a DNA triplet for seven sequences of the type GNN. Similar approaches may be applied to other **zinc fingers** to broaden the scope of the directory.

11662536 BIOSIS Number: 98262536

A conformationally homogeneous combinatorial peptide **library**

Bianchi E; Folgori A; Wallace A; Nicotra M; Acali S; Phalipon A; Barbato G; Bazzo R; Cortese R; Felici F; Pessi A

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Journal of Molecular Biology 247 (2). 1995. 154-160.

Full Journal Title: Journal of Molecular Biology

ISSN: 0022-2836

Language: ENGLISH

Print Number: Biological Abstracts Vol. 099 Iss. 012 Ref. 167454

In search for a rational way to convert the information encoded in peptide structures into peptidomimetics, major progress could be made by coupling the power of selection methods, now enormously increased in number as a result of the development of combinatorial peptide **libraries**, with the rational design of structure-inducing templates for the selectable sequences. The availability of **libraries** of peptides with predetermined structure would enable selection-driven peptidomimetic design, whereby a conformational model for the peptide pharmacophore would be directly derived from the screening, allowing the design of a suitable non-peptidic scaffold to **replace** the peptide backbone. We describe here the first example of a conformationally homogeneous combinatorial peptide **library** , which yields ligands with the expected structure upon selection. The **library** was built by randomising five positions in the alpha-helical portion of a 26 amino acid Cys-2His-2 consensus "zinc-finger" motif. Since in **zinc-fingers** metal coordination and folding are coupled, in our **library** metal-dependent binding represents a built-in control against the selection of structurally undefined sequences. The alpha-helical **library** was produced as both fusion with the pVIII protein of filamentous phage and soluble peptides by chemical synthesis, the latter enabling the expansion of the selectable repertoire by the inclusion of non-coded amino acids. The two **libraries** were independently screened with the same receptor (a monoclonal IgA reactive against the lipopolysaccharide of the human pathogen Shigella flexneri), yielding a very similar consensus. In particular, the peptides defined by both methods showed very strong, zinc-dependent binding to the IgA. The geometrical arrangement of the side-chains of the selected peptide pharmacophore was shown by circular dichroism, Co(II)-complex absorption and high-resolution NMR to be structurally invariant with respect to the parent zinc-finger.

11112516 BIOSIS Number: 97312516

In vitro selection of **zinc fingers** with altered DNA-binding specificity

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Biochemistry 33 (19). 1994. 5689-5695.

Full Journal Title: Biochemistry

ISSN: 0006-2960

Language: ENGLISH

Print Number: Biological Abstracts Vol. 098 Iss. 002 Ref. 019028

We have used random mutagenesis and phage display to alter the DNA-binding specificity of Zif268, a transcription factor that contains three zinc finger domains. Four residues in the helix of finger 1 of Zif268

that potentially mediate DNA binding were identified from an X-ray structure of the Zif268-DNA complex. A **library** was constructed in which these residues were randomly **mutated** and the Zif268 variants were fused to a truncated version of the gene III coat protein on the surface of M13 filamentous phage particles. The phage displayed the mutant proteins in a monovalent fashion and were sorted by repeated binding and elution from affinity matrices containing different DNA sequences, When the matrix contained the natural nine base pair operator sequence 5'-GCG-TGG-GCG-3', native-like **zinc fingers** were isolated. New finger 1 variants were found by sorting with two different operators in which the singly modified triplets, GTG and TCG, **replaced** the native finger 1 triplet, GCG. Overall, the selected finger 1 variants contained a preponderance of polar residues at the four sites. Interestingly, the net charge of the four residues in any selected finger never deviated more that one unit from neutrality despite the fact that about half the variants contained three or four charged residues over the four sites. Measurements of the dissociation constants for two of these purified finger 1 variants by gel-shift assay showed their specificities to vary over a 10-fold range, with the greatest affinity being for the DNA binding site for which they were sorted. We were unable to enrich for clones that bind to five other binding sites (ACG, CCG, CGC, ATA, and TAT), suggesting modification of just these four residues in finger I may not allow it to adapt to all DNA binding sites. The studies show it is possible to isolate **zinc fingers** by phage display that distinguish operator sequences that differ by a single base change. Moreover, such selection methods should aid in clarifying rules for zinc finger-DNA recognition.

8616938 EMBASE No: 92293814

Cloning of GT box-binding proteins: A novel Sp1 multigene family regulating T-cell receptor gene expression

Kingsley C.; Winoto A.

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MOL. CELL. BIOL. (USA) , 1992, 12/10 (4251-4261) CODEN: MCEBD ISSN: 0270-7306

LANGUAGES: English SUMMARY LANGUAGES: English

Analysis of a T-cell antigen receptor (TCR) alpha promoter from a variable gene segment (V) revealed a critical GT box element which is also found in upstream regions of several Valpha genes, TCR enhancer, and regulatory elements of other genes. This element is necessary for TCR gene expression and binds several proteins. These GT box-binding proteins were identified as members of a novel Sp1 multigene family. Two of them, which we term Sp2 and Sp3, were cloned. Sp2 and Sp3 contain **zinc fingers** and transactivation domains similar to those of Sp1. Like Sp1, Sp2 and Sp3 are expressed ubiquitously, and their in vitro-translated products bind to the GT box in TCR Valpha promoters. Sp3, in particular, also binds to the Sp1 consensus sequence GC box and has binding activity similar to that of Sp1. As the GT box has also previously been shown to play a role in gene regulation of other genes, these newly isolated Sp2 and Sp3 proteins might regulate expression not only of the TCR gene but of

09142176 97296423

A target of phosphatidylinositol 3,4,5-trisphosphate with a zinc finger motif similar to that of the ADP-ribosylation-factor GTPase-activating protein and two pleckstrin homology domains.

Tanaka K; Imajoh-Ohmi S; Sawada T; Shirai R; Hashimoto Y; Iwasaki S; Kaibuchi K; Kanaho Y; Shirai T; Terada Y; Kimura K; Nagata S; Fukui Y

Department of Applied Biological Chemistry, The Graduate School of Agriculture and Life Sciences, University of Tokyo, Bunkyo-ku, Japan.

Eur J Biochem (GERMANY) Apr 15 1997, 245 (2) p512-9, ISSN 0014-2956 Journal Code: EMZ

Languages: ENGLISH

Document type: JOURNAL ARTICLE

We have purified a protein that binds phosphatidylinositol

3,4,5-trisphosphate [PtdIns(3,4,5)P3] using beads bearing a PtdIns(3,4,5)P3 analogue. This protein with a molecular mass of 43 kDa, was termed PtdIns(3,4,5)P3-binding protein. The partial amino acid sequences were determined and a full-length cDNA encoding the protein was isolated from bovine brain cDNA **library**. The clone harbored an open reading frame of 373 amino acids which contained one zinc finger motif similar to that of ADP-ribosylation-factor GTPase-activating protein and two pleckstrin homology domains. The entire sequence was 83% similar to centaurin alpha, another PtdIns(3,4,5)P3-binding protein. The protein bound PtdIns(3,4,5)P3 with a higher affinity than it did inositol 1,3,4,5-tetrakisphosphate, phosphatidylinositol 4,5-bisphosphate, phosphatidylinositol 3,4-bisphosphate, and phosphatidylinositol 3-phosphate suggesting that the binding to PtdIns(3,4,5)P3 was specific. The binding activity was weaker in the mutants with a point **mutation** in the conserved sequences in each pleckstrin homology domain. Introduction of both **mutations** abolished the activity. These results suggest that this new binding protein binds PtdIns(3,4,5)P3 through two pleckstrin domains present in the molecule.

08759089 96032831

A novel DNA-binding domain that may form a single zinc finger motif.

Yanagisawa S

Department of Life Sciences (Chemistry), Graduate School of Arts and Sciences, University of Tokyo, Japan.

Nucleic Acids Res (ENGLAND) Sep 11 1995, 23 (17) p3403-10, ISSN 0305-1048 Journal Code: O8L

Languages: ENGLISH

Document type: JOURNAL ARTICLE

QP620.N8

MNB1a is a DNA-binding protein from maize that interacts with the 35S promoter of cauliflower mosaic virus. This protein did not show significant homologies with any other DNA-binding protein and MNB1a seemed to be a member of a multigene family. In this study, isolation of cDNAs from the gene family to which MNB1a belongs revealed a unique conserved domain, referred to herein as the Dof domain, that contains a novel cysteine-rich motif for a single putative zinc finger. The amino acid sequence of the Dof domain and the arrangement of cysteine residues in this domain differ from those of known zinc finger motifs. However, the Dof domain was shown to be a DNA-binding domain that required Zn2+ ions for activity. **Mutations** at cysteine residues eliminated the DNA-binding activity of MNB1a. Thus, the Dof domain may be classified as a novel zinc finger motif. In addition, Southern blot analysis and a survey of DNA databases suggested that proteins that include Dof domains might exist in other eukaryotes, at least

08728242 94119100

The Drosophila l(2)35Ba/nocA gene encodes a putative Zn finger protein involved in the development of the embryonic brain and the adult ocellar structures.

Cheah PY; Meng YB; Yang X; Kimbrell D; Ashburner M; Chia W

Drosophila Neurobiology Laboratory, National University of Singapore.

Mol Cell Biol (UNITED STATES) Feb 1994, 14 (2) p1487-99, ISSN 0270-7306 Journal Code: NGY

Languages: ENGLISH

Document type: JOURNAL ARTICLE

The Drosophila l(2)35Ba/nocA gene is involved in the development of the adult ocelli and the embryonic head. **Mutations** in this gene lead to at least two distinct phenotypes. Several larva lethal l(2)35Ba alleles cause both hypertrophy and mislocation of the embryonic supraesophageal ganglion (brain) to the dorsal surface of the embryo. A second class of mutant alleles (nocA) is homozygous viable, but the surviving adults either lack or have greatly reduced ocelli and associated bristles. The l(2)35Ba/nocA gene encodes an approximately 3.0-kb transcript doublet; all l(2)35Ba alleles which have been physically mapped delete or disrupt the transcribed region, whereas all of the viable nocA alleles are caused by gross chromosomal aberrations with breakpoints near the 3'-flanking region of the gene. Several nocA breakpoint alleles downregulate the level of

l(2)35Ba/nocA transcripts in adults, and their defective ocellar phenotype also fails to be complemented by the lethal alleles, indicating that l(2)35Ba and nocA are different phenotypic manifestations of **mutations** in the same gene. In the l(2)35Ba mutant embryos, cells from the procephalic lobe which normally migrate over and overlie the supraesophageal ganglion during head involution can become incorporated into the supraesophageal ganglion; many of these misplaced cells, which normally form the frontal sac, also adopt a neuronal fate. Sequence analysis of two full-length l(2)35Ba/nocA cDNAs with distinct polyadenylation sites shows that they encode the same deduced protein of 537 amino acids with a serine- and threonine-rich N-terminal region, two putative zinc finger motifs near the carboxyl terminus, and several alanine-rich domains. Consistent with the observed embryonic phenotype, l(2)35Ba/nocA shows a complex embryonic expression pattern which includes the procephalic lobe.

08702863 96397632
Computational screening of combinatorial **libraries**.
Zheng Q; Kyle DJ
Scios Nova, Inc., Sunnyvale, CA 94086, USA.
Bioorg Med Chem (ENGLAND) May 1996, 4 (5) p631-8, ISSN 0968-0896
Journal Code: B38
Languages: ENGLISH
Document type: JOURNAL ARTICLE
We first review existing computational methods with an intrinsic combinatorial feature, then describe a new computational method for screening combinatorial **libraries** using a recently developed multicopy sampling technique. The new method differs from the existing ones in that it can be used to screen simultaneously an entire **library** of molecules, instead of the individual molecules in a **library**. As an example, we have applied the method to study site-directed amino acid **substitutions** in a protein. After two rounds of **library** screening, we identified the energetically most stable **substitutions** along with their optimal conformations from all natural amino acids. In principle, the method is generally applicable to study ligand-host systems.

08503105 96081683
[Negative repressor THZif-1 of protooncogene c-myc]
Yokoyama K; Tsutsui H; Fujita A
RIKEN (The Institute of Physical and Chemical Research), Tsukuba Life Science Center.
Nippon Rinsho (JAPAN) Nov 1995, 53 (11) p2827-36, ISSN 0047-1852
Journal Code: KIM
Languages: JAPANESE Summary Languages: ENGLISH
Ordered 11/10/97
Document type: JOURNAL ARTICLE; REVIEW; REVIEW, TUTORIAL English Abstract
A human recombinant cDNA clone that encoded 253 amino acids residues of a zinc-finger protein (THZif-1) was cloned by screening a cDNA **library** prepared from human promyelocytic leukemia HL60 cells with synthetic oligodeoxynucleotide probes that corresponded to the amino acid sequences of tryptic peptides derived from the DNA-binding protein specific for the nuclease-hypersensitive element (NHE) of the human c-myc gene. The predicted amino acid sequence of THZif-1 included a DNA-binding domain that contained five tandemly repeated zinc finger motifs. The three amino-terminal sets of zinc finger motifs, including the second finger, were found to be responsible for high-affinity interactions with the triple-helical conformation of NHE, as well as for high-affinity binding to the single-pyrimidine-rich strand of NHE in a sequence-specific manner. Cotransfection, trans-activation and in vitro transcription studies using the wild-type form and THZif-1 with a **mutated** second zinc finger motif demonstrated that the DNA-binding activity specific for H-form DNA of NHE was a prerequisite for the negative regulation of the expression of the

08351505 95379762

The Aspergillus uvsH gene encodes a product homologous to yeast RAD18 and Neurospora UVS-2.

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Department of Microbiology, Seoul National University, Korea.

Mol Gen Genet (GERMANY) Jul 28 1995, 248 (2) p174-81, ISSN 0026-8925 Journal Code: NGP

Languages: ENGLISH

Document type: JOURNAL ARTICLE

The uvsH DNA repair gene of Aspergillus nidulans has been cloned by complementation of the uvsH77 **mutation** with a cosmid **library** containing genomic DNA inserts from a wild-type strain. Methylmethane sulfonate (MMS)-resistant transformants were obtained on medium containing 0.01% MMS, to which uvsH mutants exhibit high sensitivity. Retransformation of uvsH77 mutants with the rescued cosmids from the MMS-resistant transformants resulted in restoration of both UV and MMS resistance to wild-type levels. Nucleotide sequence analysis of the genomic DNA and cDNA of the uvsH gene shows that it has an open reading frame (ORF) of 1329 bp, interrupted by two introns of 51 and 61 bp. A 2.4 kb transcript of the uvsH gene was detected by Northern blot analysis. Primer extension analysis revealed that transcription starts at 31 bp upstream from the translation initiation codon. This gene encodes a predicted polypeptide of 443 amino acids, which has two unique zinc finger motifs. The proposed polypeptide displays 39% identity to the Neurospora crassa UVS-2 protein and 24% identity to the Saccharomyces cerevisiae RAD18 protein. The sequence similarity is particularly high in three domains. One zinc finger (RING finger) motif is located in the first domain close to the N-terminus. The other zinc finger motif is in the second domain. In the third domain, the **mutation** sites in both the uvsH77 and uvsH304 alleles were identified.(ABSTRACT TRUNCATED AT 250 WORDS)

7/3,AB/24 (Item 17 from file: 155)

DIALOG(R)File 155:MEDLINE(R)

08305132 95325643

Surface plasmon resonance based kinetic studies of zinc finger-DNA interactions.

Yang WP; Wu H; Barbas CF 3rd

Department of Molecular Biology, Scripps Research Institute, La Jolla, CA 92037, USA.

J Immunol Methods (NETHERLANDS) Jun 14 1995, 183 (1) p175-82, ISSN 0022-1759 Journal Code: IFE

Languages: ENGLISH

Document type: JOURNAL ARTICLE

Libraries of the zinc finger DNA binding protein, Zif268, have been constructed and selected for affinity and specificity toward DNA targets using the phage display technique (Wu et al., 1995). Mutant proteins were purified to homogeneity and were characterized for their ability to interact with their DNA targets using a real-time biomolecular interaction assay (BIA). One mutant protein, C7, bound the Zif268 consensus binding sequence with a 13-fold increase in affinity as compared to the wild-type Zif268 protein. Mutant proteins with moderate affinity for new DNA targets within a consensus sequence of HIV-1 have also been obtained. Surface plasmon resonance based BIA has provided invaluable kinetic information which offers insights into the mechanism of protein-DNA interactions.

8298410 95318055

Identification and functional characterization of an erythroid-specific enhancer in the L-type pyruvate kinase gene.

Lacronique V; Lopez S; Miquerol L; Porteu A; Kahn A; Raymondjean M

Institut Cochin de Genetique Moleculaire, Unite 129 INSERM, Universite Rene Descartes, Paris, France.

J Biol Chem (UNITED STATES) Jun 23 1995, 270 (25) p14989-97, ISSN 0021-9258 Journal Code: HIV

Languages: ENGLISH

Document type: JOURNAL ARTICLE

The rat L-type pyruvate kinase gene is transcribed either from promoter L in the liver or promoter L' in erythroid cells. We have now cloned and functionally characterized an erythroid-specific enhancer, mapped in the fetal liver as hypersensitive site B (HSSB) at 3.7 kilobases upstream from the promoter L'. Protein-DNA interactions were examined in the 200-base pair core of the site by in vivo footprinting experiments. In the fetal liver, footprints were revealed at multiple GATA and CACC/GT motifs, whose association is the hallmark of erythroid-specific regulatory sequences. Functional analysis of the HSSB element in transgenic mice revealed properties of a cell-restricted enhancer. Indeed, this element was able to activate the linked ubiquitous herpes simplex virus thymidine kinase promoter in erythroid tissues. The activation was also observed in a variety of nonerythroid tissues known to synthesize GATA-binding factors. In the context of L'-PK transgenes, HSSB was not needed for an erythroid-specific activation of the L' promoter, while it was required to stimulate the L' promoter activity to a proper level. Finally, HSSB cannot be **replaced** by strong ubiquitous viral or cellular enhancers, suggesting a preferential interaction of the HSSB region with the L' promoter.

08082052 95066376

A new nuclear suppressor system for a mitochondrial RNA polymerase mutant identifies an unusual zinc-finger protein and a polyglutamine domain protein in Saccharomyces cerevisiae.

Brohl S; Lisowsky T; Riemen G; Michaelis G

Botanisches Institut, Universitat Dusseldorf, Germany.

Yeast (ENGLAND) Jun 1994, 10 (6) p719-31, ISSN 0749-503X

Journal Code: YEA

Languages: ENGLISH

Document type: JOURNAL ARTICLE

A yeast strain with a point **mutation** in the nuclear gene for the core subunit of mitochondrial RNA polymerase was used to isolate new extragenic suppressors. Spontaneously occurring phenotypical revertants were analysed by crosses with the wild-type and tetrad dissection. One of the new nuclear suppressor mutants was characterized by temperature-sensitive growth on non-fermentable carbon sources. This mutant was transformed with a genomic yeast **library**. Two independent types of DNA clones were isolated which both complemented the temperature-sensitive defect. Subcloning and DNA sequencing identified two novel yeast genes which code for proteins with the characteristic features of transcription factors. Both factors exhibit highly structured protein domains consisting of runs and clusters of asparagine and glutamine residues. One of the proteins contains in addition zinc-finger domains of the C2H2-type. Therefore the genes are proposed to be named AZF1 (asparagine-rich zinc-finger protein) and PGD1 (polyglutamine domain protein). Gene disruption of both reading frames has no detectable influence on the vegetative growth on complete glucose or glycerol media, indicating that the genes may act as high copy number suppressors of the mutant defect. Additional transformation experiments showed that AZF1 is also an efficient suppressor for the original defect in the core subunit of

07883404 94185017

The ETO portion of acute myeloid leukemia t(8;21) fusion transcript encodes a highly evolutionarily conserved, putative transcription factor.

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Division of Medical Oncology, University of Colorado Health Sciences and Cancer Center, Denver 80262.

Cancer Res (UNITED STATES) Apr 1 1994, 54 (7) p1782-6, ISSN 0008-5472

Journal Code: CNF

Contract/Grant No.: P01-HD017449, HD, NICHD

Languages: ENGLISH

Document type: JOURNAL ARTICLE

The 8;21 translocation, t(8;21)(q22;q22.3), is seen only in acute myelogenous leukemia and is characteristically associated with the M2

subtype. Subsequent to our identification of the t(8;21) breakpoint region on chromosome 21, we reported that the translocation results in the fusion of the AML1 gene on chromosome 21 with a novel gene on chromosome 8 which we called ETO (for eight twenty-one). Recently, the AML1 portion of the fusion protein has been shown to correspond to the DNA-binding and dimerization domains of the mouse gene, polyoma enhancer binding protein 2 alpha B (pebp 2 alpha B). We report here the complete sequence of the ETO portion of the fusion transcript as compiled from complementary DNAs from a t(8;21) AML patient and compare this with the ETO sequence from a mouse brain transcript. The deduced amino acid sequences are 99% identical. ETO has several features consistent with it being a transcription factor. The ETO sequence is different from the portion of PEBP 2 alpha B it **replaces** in the AML1/ETO fusion protein, except for their common high content of proline, serine, and threonine residues. Because neither the putative **zinc fingers** nor the TAF110 homology domain of ETO is present in PEBP2 alpha B, one might expect functional differences in the ability of AML1/ETO protein to affect the levels of transcription of genes normally regulated to some degree by AML1 (PEBP2 alpha B) during myeloid differentiation. The relatively high levels of ETO in developing brain suggest that it could be involved in the regulation of some aspect of neural proliferation or differentiation.

7/3,AB/29 (Item 22 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

07793670 93241158

The Neurospora uvs-2 gene encodes a protein which has homology to yeast RAD18, with unique zinc finger motifs [published erratum appears in Mol Gen Genet 1994 Mar;242(6):743]

Tomita H; Soshi T; Inoue H

Department of Regulation Biology, Faculty of Science, Saitama University, Urawa, Japan.

Mol Gen Genet (GERMANY) Apr 1993, 238 (1-2) p225-33, ISSN 0026-8925 Journal Code: NGP

Languages: ENGLISH

Document type: JOURNAL ARTICLE

A clone containing the DNA repair gene uvs-2 of Neurospora crassa was identified from a Neurospora genomic DNA **library** using the sib-selection method. Transformants were screened for resistance to methyl methane sulfonate (MMS). A DNA fragment that complements the uvs-2 **mutation** was subcloned by monitoring its ability to transform the uvs-2 mutant to MMS resistance. Deletion analysis of the cloned DNA indicated that the size of the uvs-2 gene is approximately 1.6 kb. The identity of the uvs-2 gene was verified by restriction fragment length polymorphism (RFLP) mapping. The sensitivity of the transformant to three different mutagens was similar to that of the wild-type strain. Nucleotide sequences of genomic DNA and cDNA of the uvs-2 gene indicated that it has an open reading frame (ORF) of 1572 bp with a 69 bp intron in the middle of the sequence. Two transcription initiation sites located around 73 bp and 290 bp upstream of the translation initiation codon were identified by primer extension experiments. Northern analysis revealed that the nature transcript of the uvs-2 gene was about 1.8 kb long. The uvs-2 gene ORF is deduced to encode a polypeptide of 501 amino acids with a molecular mass of 54 kDa. The proposed polypeptide has 25% identity to the RAD18 polypeptide of Saccharomyces cerevisiae and contains two unique zinc finger motifs for nucleic acid binding. Similarities between the phenotypes of the rad18 and uvs-2 mutants suggest that the uvs-2 gene encodes a protein which is involved in postreplication repair, rather than excision repair.

7/3,AB/30 (Item 23 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

07682063 94040730

Perinatal lethali[redacted] and defects in hindbrain [redacted]elopment in mice homozygous for a targeted **mutation** of the zinc finger gene Krox20.

Swiatek PJ; Gridley T

Roche Institute of Molecular Biology, Roche Research Center, Nutley, New Jersey 07110.

Genes Dev (UNITED STATES) Nov 1993, 7 (11) p2071-84, ISSN 0890-9369 Journal Code: FN3

Languages: ENGLISH

Document type: JOURNAL ARTICLE

Krox20 is a zinc finger gene expressed in rhombomeres 3 and 5 during hindbrain development in vertebrates. Mice homozygous for a targeted **mutation** that deletes the majority of the Krox20 genes, including the zinc finger DNA-binding domain, died shortly after birth. The primary phenotype of the homozygous mutant animals was the loss of rhombomeres 3 and 5. This resulted in fusions of the trigeminal ganglion with the facial and vestibular ganglia, and of the superior ganglia of the glossopharyngeal and vagus nerves. These fusions resulted in a disorganization of the nerve roots of these ganglia as they entered the brain stem. These data demonstrate that Krox20 plays an essential role during development of the hindbrain and associated cranial sensory ganglia in mice.

07291220 93087555

Pur-1, a zinc-finger protein that binds to purine-rich sequences, transactivates an insulin promoter in heterologous cells.

Kennedy GC; Rutter WJ

Hormone Research Institute, University of California, San Francisco 94143-0534.

Proc Natl Acad Sci U S A (UNITED STATES) Dec 1 1992, 89 (23) p11498-502, ISSN 0027-8424 Journal Code: PV3

Contract/Grant No.: DK08132, DK, NIDDK; DK21344, DK, NIDDK

Languages: ENGLISH

Document type: JOURNAL ARTICLE

Purine-rich stretches of nucleotides (GAGA boxes) are often found just upstream of transcription start sites in many genes, including insulin. **Mutational** analysis suggests that the GAGA box plays an important role in transcription of the rat insulin I gene. We identify here at least four different proteins that bind specifically to the insulin GAGA box. Using a GAGA oligonucleotide, we have isolated a cDNA encoding a sequence-specific protein from a HIT (hamster insulinoma cell line) lambda gt11 **library** . This protein, which we designate Pur-1 (for purine binding), binds to the GAGA boxes of the rat insulin I and II genes and the human islet amyloid polypeptide gene. Pur-1 is a potent transactivator in both pancreatic and nonpancreatic cells. Furthermore, Pur-1 is able to activate an intact insulin promoter in HeLa cells, where it is normally

07112267 92236619

Expression cloning of a novel zinc finger protein that binds to the c-fos serum response element.

Attar RM; Gilman MZ

Cold Spring Harbor Laboratory, New York 11724.

Mol Cell Biol (UNITED STATES) May 1992, 12 (5) p2432-43, ISSN 0270-7306 Journal Code: NGY

Contract/Grant No.: CA45642, CA, NCI; CA46370, CA, NCI

Languages: ENGLISH

Document type: JOURNAL ARTICLE

Induction of c-fos transcription by serum growth factors requires the serum response element (SRE). The SRE is a multifunctional element which responds to several positively and negatively acting signals. To identify cellular proteins that might mediate functions of the SRE, we screened a human cDNA expression **library** with an SRE probe. We report the isolation and characterization of SRE-ZBP, a previously unidentified SRE-binding protein. SRE-ZBP is a member of the C2H2 zinc finger family of proteins exemplified by TFIIIA and the Drosophila Kruppel protein. The

seven tandemly repeated zinc finger motifs in SRE-ZBP are sufficient for high-affinity binding to the SRE. We show that SRE-ZBP is a nuclear protein and identify a candidate cellular protein encoded by the SRE-ZBP gene. Because we cannot detect any DNA-binding activity attributable to the endogenous protein, we propose that SRE-ZBP activity may be subject to posttranslational regulation. Like c-fos mRNA, SRE-ZBP mRNA is serum inducible in HeLa cells, but with slower kinetics. The role of SRE-ZBP in the regulation of c-fos transcription remains unestablished, but this protein binds to a region of the SRE where **mutations** lead to derepression.

185108 DBA Accession No.: 95-11929 PATENT
New zinc finger-nucleotide binding polypeptides - gene cloning, expression, protein engineering and phage display, for use as an antitumor or virucide agent, or in treating plants
AUTHOR: Barbas III C F; Gottesfeld J M; Wright P E
PATENT ASSIGNEE: Scripps-Res.Inst. 1995
PATENT NUMBER: WO 9519431 PATENT DATE: 950720 WPI ACCESSION NO.: 95-263862 (9534)
PRIORITY APPLIC. NO.: US 312604 APPLIC. DATE: 940928
NATIONAL APPLIC. NO.: WO 95US829 APPLIC. DATE: 950118
LANGUAGE: English
ABSTRACT: A new zinc finger-nucleotide binding protein (ZFNB) variant has at least 2 zinc finger modules that bind to a cellular DNA or RNA (e.g. an onco-promoter, virus promoter, HTLV-1 virus, HTLV-2 virus, HIV virus-1, HIV virus-2 sequence or oncogene) and modulate its function. A ZFNB protein variant may be isolated by: identifying amino acids binding to and modulating function of a 1st sequence; creating a phage display peptide **library** by polymerase chain reaction randomized **substitution** ; expressing in a host; and isolating a clone producing a variant modulating function of a 2nd sequence. A ZFNB protein gene may be tested by linking to a 1st inducible promoter in a vector with a beta-galactosidase (EC-3.2.1.23) reporter gene operably linked to a 2nd inducible promoter and a ZFNB motif, under interaction conditions, and measuring the effect of the ZFNB protein on reporter gene expression. The protein may be zif260 or TFIIIA, with a TGEKP linker between **zinc fingers**. The ZFNB protein may be used e.g. in therapy of cancer and virus-induced cell proliferative

Set	Items	Description
S1	0	SINC(W)FINGERS
S2	3870	ZINC(W)FINGERS
S3	501	ZIF268
S4	391	S2 AND LIBRAR?
S5	1006	S2 AND (SUBSTITUT? OR MUTAT? OR REPLAC?)
S6	54	S4 AND (SUBSTITUT? OR MUTAT? OR REPLAC?)

08/793,402
ATH9

1. 5,679,518, Oct. 21, 1997, Method for finding transcription activators of the NER steroid hormone receptor; Eitan Friedman, et al., 435/6, 7.1 :IMAGE AVAILABLE:

US PAT NO: 5,679,518 :IMAGE AVAILABLE: L1: 1 of 70

ABSTRACT:
The NER receptor is a novel member of the steroid hormone receptor superfamily and has been prepared by cDNA cloning from a human osteosarcoma SAOS-2/B10 cell library. The complete sequence of human NER complementary DNA (Seq. ID No. 1), expression systems including a COS stable expression system, the expressed protein (SEQ. ID No. 2) and an assay using the COS expression system are disclosed. The assay may be used to identify agents which activate transcription mediated by the NER receptor, and which are useful for potentiating the activity of a modulator of a G-protein coupled receptor wherein the G-protein coupled receptor is a member of the steroid hormone receptor superfamily.

2. 5,674,720, Oct. 7, 1997, Design and construction of non-infectious human retroviral mutants deficient in genomic RNA; Robert J. Gorelick, et al., 435/172.3; 424/188.1, 204.1, 208.1; 435/69.1; 530/350, 395 :IMAGE AVAILABLE:

US PAT NO: 5,674,720 :IMAGE AVAILABLE: L1: 2 of 70

ABSTRACT:
The present invention defines a biological role for the following sequence of amino acids that is found in the nucleocapsid domain of the gag precursor polyproteins of all replication-competent retroviruses:

-Cys-X-X-Cys-X-X-X-X-His-X-X-X-X-Cys-

wherein X represents variable amino acids. The invariant residues constitute part of a vital protein structure, at least one of which are found in all retroviruses and which are involved in the selection and packaging of genomic viral RNA into infectious virus particles. Disruption of this structure leads to the formation of virus-like particles which appear to be structurally normal, but which do not contain the normal complement of viral RNA. Therefore, their infectivity is drastically reduced or completely eliminated. The infectivity of any retrovirus, including human retroviruses, and more particularly human immunodeficiency virus (HIV), can be drastically reduced or completely eliminated by generating mutants that lack some or all of the invariant residues required to form the structure. In addition, any means of disrupting the function of this array will in turn disrupt the viral life cycle. Thus, with the knowledge provided by this invention, chemotherapeutic reagents aimed toward this array may be devised.

3. 5,670,518, Sep. 23, 1997, Aromatic nitro and nitroso compounds and their metabolites useful as anti-viral and anti-tumor agents; Ernest Kun, et al., 514/309, 456, 617; 546/141; 549/399; 564/164 :IMAGE AVAILABLE:

US PAT NO: 5,670,518 :IMAGE AVAILABLE: L1: 3 of 70

ABSTRACT:
Unsubstituted or substituted halo nitro and nitroso compounds and their metabolites are potent, selective and non-toxic inhibitors and supressants of cancer growth and viral infections in a mammalian host. The compounds are particularly useful for treatment and supression of tumors and viruses associated with breast cancer, AIDS, herpetic episodes

and cytomegaloviral infections. The methods of treatment of tumorigenic and viral diseases by [redacted]lo nitro and nitroso compounds [redacted]d their metabolites are described.

4. 5,670,317, Sep. 23, 1997, Diagnostic test for the desmoplastic small round cell tumor; Marc Ladanyi, et al., 435/6, 91.2, 91.5, 91.51; 436/64; 536/23.4, 23.5, 24.31; 935/9, 78 :IMAGE AVAILABLE:

US PAT NO: 5,670,317 :IMAGE AVAILABLE: L1: 4 of 70

ABSTRACT:
The present invention provides an isolated nucleic acid molecule encoding a chimeric EWS-WT1 protein. This invention also provides an isolated protein which is a chimeric EWS-WT1 protein. This invention further provides a method of diagnosing a desmoplastic small round cell tumor in a subject which comprises detecting in a sample from the subject a nucleic acid molecule encoding a chimeric EWS-WT1 protein, positive detection indicating the presence of desmoplastic small round cell tumor. This invention also provides a method of inhibiting the growth of a neoplastic cell, wherein the cell is characterized by the presence of a chimeric EWS-WT1 protein which comprises contacting an antibody which specifically recognizes the chimeric EWS-WT1 fusion protein under suitable conditions so that an antibody-antigen complex is formed, thereby inhibiting the growth of the neoplastic cell.

5. 5,668,291, Sep. 16, 1997, Arylthio compounds; John Michael Domagala, et al., 546/316; 564/82, 83, 86, 87, 91 :IMAGE AVAILABLE:

US PAT NO: 5,668,291 :IMAGE AVAILABLE: L1: 5 of 70

ABSTRACT:
Arylthiol and dithiobisarylamide antibacterial and antiviral agents have the general formula ##STR1## where A is monocyclic or bicyclic aryl which can contain up to 3 heteroatoms selected from O, S, and N, R.sup.1 and R.sup.2 are substituent groups, X is ##STR2## or SO.sub.2 NR.sup.4 Z, Y is H or SZ when n is 1, a single bond when n is 2; R.sup.4 and Z can be hydrogen or alkyl.

6. 5,668,004, Sep. 16, 1997, DNA polymerase III holoenzyme from Escherichia coli; Michael E. O'Donnell, 435/194, 252.3, 252.33, 320.1, 325; 530/350; 536/23.2, 23.7 :IMAGE AVAILABLE:

US PAT NO: 5,668,004 :IMAGE AVAILABLE: L1: 6 of 70

ABSTRACT:
The present invention is directed toward the 5 previously unknown genes, for subunits .delta., .delta.', .chi., .theta., and .psi., of the DNA polymerase III holoenzyme, and toward a unique man-made enzyme containing 5, preferably 6, protein subunits which shows the same activity as the naturally occurring 10 protein subunit DNA polymerase III holoenzyme.

7. 5,665,543, Sep. 9, 1997, Method of discovering chemicals capable of functioning as gene expression modulators; J. Gordon Foulkes, et al., 435/6, 69.1, 320.1; 935/77, 78 :IMAGE AVAILABLE:

US PAT NO: 5,665,543 :IMAGE AVAILABLE: L1: 7 of 70

ABSTRACT:
The present invention provides a method of transcriptionally modulating the expression of a gene-of-interest. The method comprises contacting a cell which is capable of expressing the gene with an amount of a molecule effective to transcriptionally modulate expression of the gene and thereby affect the level of the protein encoded by the gene which is expressed by the cell. Molecules useful in the practice of the invention are characterized as follows (a) do not naturally occur in the cell, (b) bind to DNA or RNA or bind to a protein through a domain of such protein

which is not a ligand binding domain of a receptor which naturally occurs in the cell. Additionally, this invention provides a method for determining whether a molecule known to be a modulator of protein biosynthesis is capable of transcriptionally modulating expression of a gene-of-interest.

8. 5,658,784, Aug. 19, 1997, Nucleic acid encoding transcription factor p300 and uses of p300; Richard Eckner, et al., 435/325, 252.3, 320.1, 366; 536/23.5, 24.31 :IMAGE AVAILABLE:

US PAT NO: 5,658,784 :IMAGE AVAILABLE: L1: 8 of 70

ABSTRACT:
The invention features an isolated nucleic acid hybridizable with the complement of the coding strand nucleic acid sequence presented in SEQ ID NO:1, and encoding a protein that is necessary for adenovirus transformation of a mammalian cell. The encoded protein, p300, cooperates with adenovirus E1A (Early-region 1A) proteins to establish the transformed state.

9. RE 35,585, Aug. 12, 1997, DNA vector with isolated cDNA gene encoding metallopanstimulin; Jose A. Fernandez-Pol, 536/23.5; 435/69.1, 69.7, 252.3, 325, 348; 536/24.31 :IMAGE AVAILABLE:

US PAT NO: RE 35,585 :IMAGE AVAILABLE: L1: 9 of 70

ABSTRACT:
A novel DNA sequence is disclosed which encodes a protein associated with many human cancers. This protein is designated as metallopanstimulin-1 (MPS-1) since (1) it is associated with metal ions, particularly zinc; (2) it has been detected in numerous different types of cells; (3) it is associated with rapid cell proliferation. The MPS-1 mRNA and its encoded protein are expressed in normal cells to a much lesser degree than in premalignant or malignant tumor cells, and they are present at very low levels in senescent cells compared to young healthy cells. The DNA sequence and the protein can be used in diagnostic methods such as detection of malignant cells associated with several types of tumors. Thus, this invention discloses a method for determining the presence of certain types of malignant conditions in patients. The MPS-1 cDNA sequence has been inserted into convenient vectors, and a culture of E. coli cells containing the sequence has been deposited with the American Type Culture Collection (ATCC), under accession number ATCC 68656.

10. 5,654,151, Aug. 5, 1997, High affinity HIV Nucleocapsid nucleic acid ligands; Patrick Nikita Allen, et al., 435/6, 91.2; 536/23.1; 935/77, 78 :IMAGE AVAILABLE:

US PAT NO: 5,654,151 :IMAGE AVAILABLE: L1: 10 of 70

ABSTRACT:
Methods are described for the identification and preparation of high-affinity nucleic acid ligands to HIV-1 nucleocapsid. Included in the invention are specific RNA ligands to HIV-1 nucleocapsid identified by the SELEX method. Also included are RNA ligands that inhibit the function of HIV-1 nucleocapsid.

11. 5,652,367, Jul. 29, 1997, Halo-nitro-isoquinolinone compounds and pharmaceutical compositions thereof; Ernest Kun, et al., 546/141, 142 :IMAGE AVAILABLE:

US PAT NO: 5,652,367 :IMAGE AVAILABLE: L1: 11 of 70

ABSTRACT:
Unsubstituted or substituted halo nitro and nitroso compounds and their metabolites are potent, selective and non-toxic inhibitors and supressants of cancer growth and vital infections in a mammalian host.

The compounds are particularly useful for treatment and supression of tumors and viruses associated with breast cancer, AIDS herpetic episodes and cytomegaloviral infections. The methods of treatment of tumorigenic and vital diseases by halo nitro and nitroso compounds and their metabolites are described.

12. 5,652,340, Jul. 29, 1997, Matrix-associating DNA-binding protein, nucleic acids encoding the same and methods for detecting the nucleic acids; Terumi Kohwi-Shigematsu, et al., 530/358 :IMAGE AVAILABLE:

US PAT NO: 5,652,340 :IMAGE AVAILABLE: L1: 12 of 70

ABSTRACT:
The present invention provides a novel human protein, SATB1, that binds matrix/scaffold-associating DNA regions (MARs). The novel human protein, predominantly expressed in the thymus, has an approximate molecular weight of about 85.9 kD. The SATB1 cDNA encodes a 763 amino acid sequence protein that is capable of binding to special AT rich sequences (ATC sequences). The invention further provides antibodies specifically reactive with such protein. Isolated nucleic acids encoding the novel MAR-binding protein are also provided, as well as vectors containing the nucleic acids and recombinant host cells transformed with such vectors. The invention further provides methods of detecting such nucleic acids by contacting a sample with a nucleic acid probe having a nucleotide sequence capable of hybridizing with the isolated nucleic acids of the present invention. Such probes can correspond to the ATC sequences.

13. 5,652,260, Jul. 29, 1997, Adenosine diphosphoribose polymerase binding nitroso aromatic compound useful as retroviral inactivating agents, anti-retroviral agents and anti-tumor agents; Ernest Kun, et al., 514/457, 309, 617, 619, 620; 546/141; 549/288; 564/163, 164, 166 :IMAGE AVAILABLE:

US PAT NO: 5,652,260 :IMAGE AVAILABLE: L1: 13 of 70

ABSTRACT:
The subject invention provides for novel compounds for inactivating viruses. These compounds include 6-nitroso-1,2-benzopyrone, 3-nitrosobenzamide, 5-nitroso-1(2H)-isoquinolinone, 7-nitroso-1(2H)-isoquinolinone, 8-nitroso-1(2H)-isoquinolinone. The invention also provides for compositions containing one or more of the compounds, and for methods of treating viral infections, cancer, infectious virus concentration with the subject compounds and compositions.

14. 5,650,550, Jul. 22, 1997, Mutant mice having a deficit of functional estrogen receptors; Kenneth S. Korach, et al., 800/2; 435/172.3, 354; 800/DIG.1; 935/10, 70 :IMAGE AVAILABLE:

US PAT NO: 5,650,550 :IMAGE AVAILABLE: L1: 14 of 70

ABSTRACT:
The present invention provides a mutant non-human vertebrate, in which all or some of the germ and somatic cells contain a mutation in at least one steroid hormone receptor allele, which mutation is introduced into the vertebrate, or an ancestor of the vertebrate, at an embryonic stage, and which mutation produces a phenotype in the vertebrate characterized by a deficit of functional steroid hormone receptors encoded by the allele. Also disclosed are related methods and constructs.

15. 5,641,652, Jun. 24, 1997, Insect retinoid-like receptor compositions and methods; Anthony E. Oro, et al., 435/69.1; 530/350 :IMAGE AVAILABLE:

US PAT NO: 5,641,652 :IMAGE AVAILABLE: L1: 15 of 70

ABSTRACT:
The present invention relates to the discovery of novel insect receptor

polypeptides, which, when complexed with certain ligands or otherwise activated by certain compounds, modulate transcription of certain genes by binding to cognate response elements associated with the promoters of the genes. The novel receptors of the invention are substantially similar to previously discovered mammalian receptors which are activated to modulate transcription of certain genes in cells, when the cells are exposed to retinoic acid. The invention provides DNAs encoding the novel receptors, including expression vectors for expression of the receptors in cells; cells transformed with such expression vectors; cells co-transformed with such expression vectors and with reporter vectors to monitor activation of the receptors to modulate transcription, when the cells are exposed to ligand for the invention receptor; and methods of using such co-transformed cells in screening for compounds which are capable of leading to activation of the receptors and for compounds which are capable of interfering with such activation and, as such, are potentially potent insecticides. The invention also provides DNA and RNA probes for identifying DNA's encoding related receptors, of insects and other animals, of the class, to which the novel receptors of the invention belong.

16. 5,639,616, Jun. 17, 1997, Isolated nucleic acid encoding a ubiquitous nuclear receptor; Shutsung Liao, et al., 435/7.1, 69.1, 252.3, 320.1; 536/23.5, 24.3 :IMAGE AVAILABLE:

US PAT NO: 5,639,616 :IMAGE AVAILABLE: L1: 16 of 70

ABSTRACT:
The invention relates generally to compositions of and methods for obtaining ubiquitous, nuclear receptor (UR) polypeptides. The invention also relates to polynucleotides encoding UR polypeptides, recombinant host cells and vectors containing UR-encoding polynucleotide sequences, and recombinant UR polypeptides. By way of example, the invention discloses the cloning and functional expression of at least two different UR polypeptides. The invention also includes methods for using the isolated, recombinant receptor polypeptides in assays designed to select substances which interact with UR polypeptides for use in diagnostic, drug design and therapeutic applications.

17. 5,637,686, Jun. 10, 1997, Tata-binding protein associated factor, nucleic acids; Robert Tjian, et al., 536/23.5, 23.1 :IMAGE AVAILABLE:

US PAT NO: 5,637,686 :IMAGE AVAILABLE: L1: 17 of 70

ABSTRACT:
TATA-binding protein associated factors, TAFs, nuclear proteins involved in RNA polymerase I, II, and III transcription, and nucleic acids encoding TAFs are disclosed. The disclosed methods and compositions find use in developing pharmaceuticals, diagnosis and therapy.

18. 5,637,311, Jun. 10, 1997, Zinc(II) complexes and methods related thereto; Alexander J. Pallenberg, 424/434, 433, 435, 436, 443, 489, 641; 514/332; 556/134, 135 :IMAGE AVAILABLE:

US PAT NO: 5,637,311 :IMAGE AVAILABLE: L1: 18 of 70

ABSTRACT:
Zinc(II) complexes and methods relating thereto are disclosed. The zinc(II) complexes comprise a zinc(II) ion complexed by a multi-dentate ligand. Methods of this invention include the use of the zinc(II) complexes as anti-viral agents and/or as anti-inflammatory agents. Methods of this invention also include inhibition of viral infection, as well as inhibiting transmission of sexually transmitted diseases. Exemplary zinc(II) complexes include zinc(II):neocuproine (2:1) and zinc(II):bathocuproine disulfonic acid (2:1).

19. 5,635,615, Jun. 3, 1997, High affinity HIV nucleocapsid nucleic acid

ligands; Patrick Aller et al., 536/22.1; 435/6, 91.2; 935/77, 78 :IMAGE AVAILABLE:

US PAT NO: 5,635,615 :IMAGE AVAILABLE: L1: 19 of 70

ABSTRACT:
Methods are described for the identification and preparation of high-affinity nucleic acid ligands to HIV-1 nucleocapsid. Included in the invention are specific RNA ligands to HIV-1 nucleocapsid identified by the SELEX method and RNA ligands that inhibit the function of HIV-1 nucleocapsid.

20. 5,633,142, May 27, 1997, WT1 monoclonal antibodies and methods of use therefor; Meenhard Herlyn, et al., 435/7.23, 7.1, 7.2, 7.21; 530/387.1, 387.7, 388.1, 388.8, 809 :IMAGE AVAILABLE:

US PAT NO: 5,633,142 :IMAGE AVAILABLE: L1: 20 of 70

ABSTRACT:
The present invention provides three unique monoclonal antibodies directed against a portion of the Wilms' tumor antigen, and methods of use therefor in detecting, monitoring and diagnosing malignancies characterized by over-expression or inappropriate expression of the WT 1 protein.

21. 5,633,136, May 27, 1997, ALL-1 polynucleotides for leukemia detection and treatment; Carlo Croce, et al., 435/6, 91.2; 536/23.1, 24.3, 24.31, 24.33 :IMAGE AVAILABLE:

US PAT NO: 5,633,136 :IMAGE AVAILABLE: L1: 21 of 70

ABSTRACT:
Methods are provided for the diagnosis and treatment of human leukemias involving breakpoints on chromosome 11 in the ALL-1 locus. The ALL-1 breakpoint region, an approximately 8 kb region on chromosome 11 is also disclosed. The ALL-1 region is involved in translocations in acute lymphocytic, mylemonocytic, monocytic, and myelogenous leukemias. Probes which identify chromosome aberrations involving the ALL-1 breakpoint region on chromosome 11 are also provided. The cDNA sequence of the ALL-1 gene on chromosome 11 is provided. A partial sequence of the AF-4 gene is also provided in the context of the sequences of the two reciprocal end products of a translocation. Amino acid sequences corresponding to the cDNA sequences of the entire ALL-1 gene and the partial sequence of the AF-4 gene are also provided. Probes are provided for detecting chromosomal abnormalities involving the ALL-1 gene on chromosome 11. Monoclonal antibodies for diagnosis and treatment and antisense oligonucleotides for the treatment of acute leukemias are also described.

22. 5,633,135, May 27, 1997, Chimeric nucleic acids and proteins resulting from ALL-1 region chromosome abnormalities; Carlo Croce, et al., 435/6, 91.2; 536/24.31, 24.33; 935/8, 78 :IMAGE AVAILABLE:

US PAT NO: 5,633,135 :IMAGE AVAILABLE: L1: 22 of 70

ABSTRACT:
Methods are provided for the diagnosis and treatment of human leukemias involving breakpoints on chromosome 11 in the ALL-1 locus. The ALL-1 breakpoint region, an approximately 8 kb region on chromosome 11, is also disclosed. The ALL-1 region is involved in translocations in acute lymphocytic, myelomonocytic, monocytic and myelogenous leukemias. Probes which identify chromosome aberrations involving the ALL-1 breakpoint region on chromosome 11 are also provided. cDNA sequences of the ALL-1 gene on chromosome 11, the AF-9 gene on chromosome 9 and the AF-4 gene, and corresponding amino acid sequences are also provided. Probes are provided for detecting chromosome abnormalities involving theses genes. Chimeric genes involved in translocations are disclosed. Monoclonal

antibodies for diagnosis and treatment and antisense oligonucleotides for treatment of acute leukemias are also described.

23. 5,627,024, May 6, 1997, Lambdoid bacteriophage vectors for expression and display of foreign proteins; Ichiro Maruyama, et al., 435/5, 6, 172.3, 320.1; 536/23.4 :IMAGE AVAILABLE:

US PAT NO: 5,627,024 :IMAGE AVAILABLE: L1: 23 of 70

ABSTRACT:
Lambdoid phage comprising a matrix of proteins encapsulating a genome encoding first and second polypeptides of an autogenously assembling receptor and a receptor comprised of the first and second polypeptides surface-integrated into the matrix via a lambdoid phage tail protein matrix anchor domain fused to at least one of the polypeptides.

24. 5,625,033, Apr. 29, 1997, Totally synthetic affinity reagents; Brian K. Kay, et al., 530/324; 435/7.1, 7.2, 69.1, 69.7, 172.3, 252.3, 320.1; 530/300, 350; 536/23.1, 23.5 :IMAGE AVAILABLE:

US PAT NO: 5,625,033 :IMAGE AVAILABLE: L1: 24 of 70

ABSTRACT:
A novel method for producing novel and/or improved heterofunctional binding fusion proteins termed Totally Synthetic Affinity Reagents (TSARs) is disclosed. TSARs are concatenated heterofunctional proteins, polypeptides or peptides comprising at least two functional regions: a binding domain with affinity for a ligand and a second effector peptide portion that is chemically or biologically active. In one embodiment, the heterofunctional proteins, polypeptides or peptides further comprise a linker peptide portion between the binding domain and the second active peptide portion. The linker peptide can be either susceptible or not susceptible to cleavage by enzymatic or chemical means. Novel and/or improved heterofunctional binding reagents as well as methods for using the reagents for a variety of in vitro and in vivo applications are also disclosed.

25. 5,622,835, Apr. 22, 1997, WT1 monoclonal antibodies; Meenhard Herlyn, et al., 435/328, 70.21, 172.2, 331, 344, 344.1; 530/387.3, 387.9, 388.1, 388.8, 388.85 :IMAGE AVAILABLE:

US PAT NO: 5,622,835 :IMAGE AVAILABLE: L1: 25 of 70

ABSTRACT:
Three unique monoclonal antibodies, each having an epitope located in amino acids 1-181 of the WT1 tumor protein, and the hybridomas which secrete them have been constructed. These monoclonal antibodies are useful in the detection, monitoring, and diagnosis of malignancies characterized by inappropriate expression of the WT1 protein.

26. 5,620,997, Apr. 15, 1997, Isothiazolones; Gary L. Bolton, et al., 514/373; 544/278; 546/83, 114; 548/209 :IMAGE AVAILABLE:

US PAT NO: 5,620,997 :IMAGE AVAILABLE: L1: 26 of 70

ABSTRACT:
Isothiazolones having the general structure ##STR1## where A is a monocyclic or bicyclic ring which may contain up to 3 heteroatoms selected from O, S, and N; R.sup.1 and R.sup.2 are substituent groups such as alkyl, alkoxy, hydroxy, nitro, cyano, amino, and carboxy; and R.sup.5 is alkyl, cycloalkyl, phenyl, and Het. The isothiazolones are useful as anti-retroviral agents, anti-inflammatory agents, and anti-atherosclerotic agents.

27. 5,616,699, Apr. 1, 1997, Coding, promoter and regulator sequences of IRF-1; Tadatsugu Taniguchi, et al., 536/23.1; 435/91.1; 935/1, 3, 6, 33,

34, 36, 78 :IMAGE AVAILABLE:

US PAT NO: 5,616,699 :IMAGE AVAILABLE: L1: 27 of 70

ABSTRACT:
A recombinant DNA molecule coding for a protein having the activity of an interferon regulatory factor-1 (IRF-1).

28. 5,614,620, Mar. 25, 1997, DNA binding proteins including androgen receptor; Shutsung Liao, et al., 536/23.5; 435/172.3, 252.33, 320.1, 325; 536/23.1; 935/11, 24, 29, 73 :IMAGE AVAILABLE:

US PAT NO: 5,614,620 :IMAGE AVAILABLE: L1: 28 of 70

ABSTRACT:
Disclosed are DNA sequences encoding DNA binding polypeptides including androgen receptor (AR) and TR2 polypeptides. Illustratively, human and rat AR-cDNA have 79 kD and 98 kD polypeptide expression products which are immunoprecipitable by human auto-immune anti-androgen receptor antibodies and are capable of binding androgens specifically and with high affinity. Also disclosed are antibodies and immunological methods and materials for detection of androgen receptor and TR2 polypeptides and hybridization methods and materials for detection of AR-and TR2-related nucleic acids.

29. 5,607,967, Mar. 4, 1997, Treatment of alzheimer's disease with 5-(tetradecyloxy)-2-furan carboxylic acid; Eitan Friedman, et al., 514/461, 473 :IMAGE AVAILABLE:

US PAT NO: 5,607,967 :IMAGE AVAILABLE: L1: 29 of 70

ABSTRACT:
Use of the novel receptor NER TOFA (5-(tetradecyloxy)-2-furan-carboxylic acid) to treat Alzheimer's disease.

30. 5,604,115, Feb. 18, 1997, Liver enriched transcription factor; Frances M. Sladek, et al., 435/69.1, 252.3, 254.11, 320.1, 325, 348; 536/23.5 :IMAGE AVAILABLE:

US PAT NO: 5,604,115 :IMAGE AVAILABLE: L1: 30 of 70

ABSTRACT:

HNF-4 (hepatocyte nuclear factor 4) is a protein enriched in liver extracts that binds to sites required for the transcription of the transthyretin (TTR) and apolipoprotein CIII (apoCIII) genes (Costa et al., 1989; Costa et al., 1990; Leff et al., 1989). We have purified HNF-4 protein (54 kD) and isolated a cDNA clone encoding the protein. HNF-4 is a member of the steroid hormone receptor superfamily with an unusual amino acid in the conserved "knuckle" of the first zinc finger (DGCKG). This and the fact that HNF-4 does not bind significantly to estrogen, thyroid hormone or glucocorticoid response elements indicate that HNF-4 may represent a new subfamily. HNF-4 binds to its recognition site as a dimer and activates transcription in a sequence-specific fashion in nonhepatic (HeLa) cells. HNF-4 mRNA is present in kidney and intestine as well as liver but is absent in other tissues. DNA binding data suggest that HNF-4 could be identical to liver factor A1 (LF-A1), a factor previously shown to regulate the transcription of the .alpha.-1 antitrypsin, apolipoprotein A1 and pyruvate kinase genes.

31. 5,597,719, Jan. 28, 1997, Interaction of RAF-1 and 14-3-3 proteins; Ellen Freed, et al., 435/194 :IMAGE AVAILABLE:

US PAT NO: 5,597,719 :IMAGE AVAILABLE: L1: 31 of 70

ABSTRACT:

Intermolecular interactions between Raf-1 and human 14-3-3 proteins which regulate Raf activity are identified. Compositions and method for identifying novel drugs which modulate Raf activity in vivo are provided.

32. 5,597,693, Jan. 28, 1997, Hormone response element compositions and assay; Ronald M. Evans, et al., 435/6, 69.7; 530/330, 350 :IMAGE AVAILABLE:

US PAT NO: 5,597,693 :IMAGE AVAILABLE: L1: 32 of 70

ABSTRACT:
The present invention discloses steroid/thyroid hormone receptor DNA binding domain compositions that determine target gene specificity. The invention further discloses methods converting the target gene specificity of one receptor into the target gene specificity of another. Still further the invention discloses novel assays for identifying ligands for orphan hormone receptors. These assays are especially useful since they avoid the necessity of constructing chimeric genes and proteins in order to search for ligands that can activate a putative receptor.

33. 5,583,155, Dec. 10, 1996, 6-amino-1,2-benzopyrones useful for treatment of viral diseases; Ernest Kun, et al., 514/457, 456 :IMAGE AVAILABLE:

US PAT NO: 5,583,155 :IMAGE AVAILABLE: L1: 33 of 70

ABSTRACT:
Unsubstituted or substituted 6-amino-1,2-benzopyrones are potent, selective and non-toxic inhibitors and suppressants of viral infections in a mammalian host. The compounds are particularly useful for treatment of AIDS, herpetic episodes and cytomegaloviral infections. The method of treatment of viral diseases by 6-amino-1,2-benzopyrones is described.

34. 5,578,483, Nov. 26, 1996, Receptor transcription-repression activity compositions and methods; Ronald M. Evans, et al., 435/325, 320.1, 353, 354; 530/350 :IMAGE AVAILABLE:

US PAT NO: 5,578,483 :IMAGE AVAILABLE: L1: 34 of 70

ABSTRACT:
Disclosed is an analysis of domains of receptors of the steroid/thyroid hormone superfamily, and particularly of the glucocorticoid receptor, to identify requirements for the trans-acting transcriptional repression activities of the receptors. Based on the analysis, certain novel receptor analogs are provided, as are various novel DNAs, expression vectors, cells and transgenic animals as well as novel methods of using trans-acting transcription-repressing analogs of the receptors in various applications. These applications include gene therapy, screening of cells in culture or transgenic animals for compositions effective to treat various diseases due to inability to properly respond to hormones of the steroid or thyroid hormone group, and screening of cells in culture for ligands that are capable, upon binding to one of the receptors, to activate its trans-acting transcription activating and trans-acting transcription-repressing activities.

35. 5,574,022, Nov. 12, 1996, Method of attenuating physical damage to the spinal cord; Eugene Roberts, et al., 514/54, 165, 169, 171, 177, 178, 182, 885; 536/123.1 :IMAGE AVAILABLE:

US PAT NO: 5,574,022 :IMAGE AVAILABLE: L1: 35 of 70

ABSTRACT:
A method is disclosed for attenuation of nervous system damage after injury which comprises administering therapeutic amounts of PREG, PREG-S, or esters of PREG or PREG-S together with an enhancer of secretory

processes in non-neur[redacted]cells such as a bacterial lipop[redacted]lysaccharide and a non-steroidal antii[redacted]ammatory substance such as ind[redacted]thacin.

36. 5,571,791, Nov. 5, 1996, Modified polypeptide fragments of the glucocorticoid receptor; E. Brad Thompson, et al., 514/12; 435/69.1; 530/300 :IMAGE AVAILABLE:

US PAT NO: 5,571,791 :IMAGE AVAILABLE: L1: 36 of 70

ABSTRACT:
A cell lysis factor which is a modified fragment of the human glucocorticoid receptor. The modified fragment designated 398-465*, when transfected into and expressed in a host cell, effects cell lysis and cell death. A pharmaceutical composition having the modified fragment 398-465* or the encoded protein product may be used in treatment of proliferative diseases.

37. 5,571,698, Nov. 5, 1996, Directed evolution of novel binding proteins; Robert C. Ladner, et al., 435/69.7, 6, 69.1, 172.3, 252.3, 320.1 :IMAGE AVAILABLE:

US PAT NO: 5,571,698 :IMAGE AVAILABLE: L1: 37 of 70

ABSTRACT:
In order to obtain a novel binding protein against a chosen target, DNA molecules, each encoding a protein comprising one of a family of similar potential binding domains and a structural signal calling for the display of the protein on the outer surface of a chosen bacterial cell, bacterial spore or phage (genetic package) are introduced into a genetic package. The protein is expressed and the potential binding domain is displayed on the outer surface of the package. The cells or viruses bearing the binding domains which recognize the target molecule are isolated and amplified. The successful binding domains are then characterized. One or more of these successful binding domains is used as a model for the design of a new family of potential binding domains, and the process is repeated until a novel binding domain having a desired affinity for the target molecule is obtained. In one embodiment, the first family of potential binding domains is related to bovine pancreatic trypsin inhibitor, the genetic package is M13 phage, and the protein includes the outer surface transport signal of the M13 gene III protein.

38. 5,571,696, Nov. 5, 1996, Receptors; Ronald M. Evans, et al., 435/69.1, 320.1, 325; 536/23.1, 23.4 :IMAGE AVAILABLE:

US PAT NO: 5,571,696 :IMAGE AVAILABLE: L1: 38 of 70

ABSTRACT:
Novel members of the steroid/thyroid superfamily of receptors are described. DNA sequences encoding same, expression vectors containing such DNA and host cells transformed with such expression vectors are also disclosed, as are methods for the expression of the novel receptors of the invention, and various uses thereof.

39. 5,552,529, Sep. 3, 1996, Autoantigen, pinch; Ann Rearden, 530/380; 424/185.1; 530/327, 806, 829 :IMAGE AVAILABLE:

US PAT NO: 5,552,529 :IMAGE AVAILABLE: L1: 39 of 70

ABSTRACT:
A novel autoantigenic polypeptide, PINCH, polynucleotides and antibodies that bind to PINCH are provided. A method for removing autoantibodies that bind to an epitope contained in PINCH from a sample, such as blood, and a method of treating autoimmune disorders associated with autoantibodies that bind an epitope in PINCH are also provided.

40. 5,539,085, Jul. 23, 1996, Bcl-2 and R-ras complex; James R.

Bischoff, et al., 530/350; 435/69.1; 530/402 :IMAGE AVAILABLE:

US PAT NO: 5,539,[illegible] :IMAGE AVAILABLE: L1: 40 of 70

ABSTRACT:
The invention provides compositions and methods for screening for agents which are modulators of bcl-2 function and can modulate bcl-2-mediated apoptosis and/or modulate neoplastic and immune conditions dependent upon bcl-2 function. The invention also provides a composition comprising a substantially pure protein complex comprising a R-ras polypeptide and a bcl-2 polypeptide.

41. 5,534,542, Jul. 9, 1996, Methods and materials relating to a bi-metallic cross-linking species; Thomas V. O'Halloran, et al., 514/492, 6, 496, 501; 556/28, 136, 137 :IMAGE AVAILABLE:

US PAT NO: 5,534,542 :IMAGE AVAILABLE: L1: 41 of 70

ABSTRACT:
Disclosed herein is a bi-metallic cross-linking reagent according to the following formula: ##STR1## where M.sub.1 is a metal ion species capable of forming a complex of coordination number four or coordination number six; wherein L.sub.1, L.sub.2, L.sub.3, and L.sub.4 are each independently a halide, ammonia, dimethyl sulfoxide, carboxylate, thiolate, imidazole, a nucleobase, or an empty coordination site, provided that no more than two of L.sub.1, L.sub.2, L.sub.3, and L.sub.4 are empty coordination sites; wherein M.sub.2 is a metal ion species capable of forming a complex of coordination number two with a first ligand that is a hydrocarbon moiety and a second ligand that is kinetically lablie; and wherein n is an integer from two to nine. Also disclosed are cross-linked species, methods of preparing the crosslinking reagents of the invention, and methods for their use in tissue-specific targeting of anti-tumor agents.

42. 5,534,410, Jul. 9, 1996, TATA-binding protein associated factors drug screens; Robert Tjian, et al., 435/6, 7.1 :IMAGE AVAILABLE:

US PAT NO: 5,534,410 :IMAGE AVAILABLE: L1: 42 of 70

ABSTRACT:
TATA-binding protein associated factors, TAFs, nuclear proteins involved in RNA polymerase I, II, and III transcription, and nucleic acids encoding TAFs are disclosed. The disclosed methods and compositions find use in developing pharmaceuticals, diagnosis and therapy.

43. 5,527,682, Jun. 18, 1996, DNA sequences encoding proteins used to elicit and detect programmed cell death; Gregory P. Owens, et al., 435/6, 252.3, 325; 536/23.5 :IMAGE AVAILABLE:

US PAT NO: 5,527,682 :IMAGE AVAILABLE: L1: 43 of 70

ABSTRACT:
Polypeptides and mutants and variants associated with programmed cell death in mammalian cells and DNA sequences, and fragments and derivatives thereof, encoding the polypeptides are disclosed. Also disclosed are methods for detecting programmed cell death in mammalian cells, a method of activating programmed cell death in unwanted mammalian cells, and methods for preventing unwanted cell death occurring in degenerative disorders of mammals.

44. 5,519,053, May 21, 1996, 5-Iodo-6-amino-1,2-Benzopyrones and their metabolites useful as cytostatic agents; Ernest Kun, et al., 514/457, 934 :IMAGE AVAILABLE:

US PAT NO: 5,519,053 :IMAGE AVAILABLE: L1: 44 of 70

ABSTRACT:
Unsubstituted or substituted 5-iodo-6-amino-1,2-benzopyrones and their metabolites are potent, selective and non-toxic inhibitors and supressants of cancer growth and viral infections in a mammalian host. The compounds are particularly useful for treatment and supression of tumors and viruses associated with AIDS, herpetic episodes and cytomegaloviral infections. The methods of treatment of tumorigenic and viral diseases by 5-iodo-6-amino-1,2-benzopryrones and/or its metabolites are described.

45. 5,516,941, May 14, 1996, Specific inactivators of "retroviral" (asymmetric) **zinc fingers**; Ernest Kun, et al., 564/166 :IMAGE AVAILABLE:

US PAT NO: 5,516,941 :IMAGE AVAILABLE: L1: 45 of 70

ABSTRACT:
The subject invention provides for novel compounds for inactivating viruses. These compounds include 6-nitroso-1,2-benzopyrone, 3-nitrosobenzamide, 5-nitroso-1(2H)isoquinolinone, 7-nitroso-1(2H)-isoquinolinone, 8-nitroso-1(2H)-isoquinolinone. The invention also provides for compositions containing one or more of the compounds, and for methods of treating viral infections, cancer, infectious virus concentration with the subject compounds and compositions.

46. 5,514,578, May 7, 1996, Polynucleotides encoding insect steroid hormone receptor polypeptides and cells transformed with same; David S. Hogness, et al., 435/325, 252.3, 348; 536/23.5 :IMAGE AVAILABLE:

US PAT NO: 5,514,578 :IMAGE AVAILABLE: L1: 46 of 70

ABSTRACT:
Polynucleotide sequences which encode ecdysone receptors have been isolated and expressed in host cells.

47. 5,512,483, Apr. 30, 1996, Expression vectors responsive to steroid hormones; Sylvie Mader, et al., 435/320.1; 536/24.1 :IMAGE AVAILABLE:

US PAT NO: 5,512,483 :IMAGE AVAILABLE: L1: 47 of 70

ABSTRACT:
Expression vector adapted for expression of cloned genes in an animal cell comprising a steroid responsive promoter, the promoter consisting essentially of a plurality of glucocorticoid response elements (GREs), a TATA box, and an initiator element containing a transcriptional initiator site located from 20 to 50 bases from the TATA box, the promoter lacking upstream elements which bind nuclear factor I, and the vector further comprising a restriction endonuclease site downstream from the promoter for insertion of DNA to be expressed from the promoter, wherein the DNA is expressed from the vector in an animal cell.

48. 5,500,356, Mar. 19, 1996, Method of nucleic acid sequence selection; Wu-Bo Li, et al., 435/91.1, 91.2, 172.3; 536/24.3, 24.33 :IMAGE AVAILABLE:

US PAT NO: 5,500,356 :IMAGE AVAILABLE: L1: 48 of 70

ABSTRACT:
The present invention provides a method for the rapid isolation and recovery of a desired target DNA or RNA molecules from a mixture or library containing such molecules. The method involves the use of biotinylated probes and enzymatic repair-cleavage to eliminate undesired library members from a sample.

49. 5,498,538, Mar. 12, 1996, Totally synthetic affinity reagents; Brian K. Kay, et al., 435/69.1, 69.7, 172.3; 536/23.4 :IMAGE AVAILABLE:

US PAT NO: 5,498,53[redacted] IMAGE AVAILABLE: L[redacted]49 of 70

ABSTRACT:
A novel method for producing novel and/or improved heterofunctional binding fusion proteins termed Totally Synthetic Affinity Reagents (TSARs) is disclosed. TSARs are concatenated heterofunctional proteins, polypeptides or peptides comprising at least two functional regions: a binding domain with affinity for a ligand and a second effector peptide portion that is chemically or biologically active. In one embodiment, the heterofunctional proteins, polypeptides or peptides further comprise a linker peptide portion between the binding domain and the second active peptide portion. The linker peptide can be either susceptible or not susceptible to cleavage by enzymatic or chemical means. Novel and/or improved heterofunctional binding reagents as well as methods for using the reagents for a variety of in vitro and in vivo applications are also disclosed.

50. 5,498,530, Mar. 12, 1996, Peptide library and screening method; Peter J. Schatz, et al., 435/69.1, 6, 172.3, 320.1 :IMAGE AVAILABLE:

US PAT NO: 5,498,530 :IMAGE AVAILABLE: L1: 50 of 70

ABSTRACT:
A random peptide library constructed by transforming host cells with a collection of recombinant vectors that encode a fusion protein comprised of a DNA binding protein and a random peptide and also contain a binding site for the DNA binding protein can be used to screen for novel ligands. The screening method results in the formation of a complex comprising the fusion protein bound to a receptor through the random peptide ligand and to the recombinant DNA vector through the DNA binding protein.

51. 5,484,951, Jan. 16, 1996, 5-iodo-6-amino-6-nitroso-1,2-benzopyrones useful as cytostatic and antiviral agents; Ernest Kun, et al., 549/285, 288, 289 :IMAGE AVAILABLE:

US PAT NO: 5,484,951 :IMAGE AVAILABLE: L1: 51 of 70

ABSTRACT:
Unsubstituted or substituted 5-iodo-6-amino-1,2-benopyrones and their metabolites are potent, selective and non-toxic inhibitors and suppressants of cancer growth and viral infections in a mammalian host. The compounds are particularly useful for treatment and suppression of tumors and viruses associated with AIDS, herpetic episodes and cytomegaloviral infections. The methods of treatment of tumorigenic and viral diseases by 5-iodo-6-amino-1,2-benzopyrones and/or its metabolites are described.

52. 5,482,975, Jan. 9, 1996, Adenosine diphosphoribose polymerase binding nitroso aromatic compounds useful as retroviral inactivating agents, anti-retroviral agents and anti-tumor agents; Ernest Kun, et al., 514/619; 564/163, 166 :IMAGE AVAILABLE:

US PAT NO: 5,482,975 :IMAGE AVAILABLE: L1: 52 of 70

ABSTRACT:
The subject invention provides for novel compounds for inactivating viruses. These compounds include 6-nitroso-1,2-benzopyrone, 3-nitrosobenzamide, 5-nitroso-1(2H)-isoquinolinone, 7-nitroso-1(2H)isoquinolinone, 8-nitroso-1(2H)isoquinolinone. The invention also provides for compositions containing one or more of the compounds, and for methods of treating viral infections, cancer, infectious virus concentration with the subject compounds and compositions.

53. 5,473,074, Dec. 5, 1995, Adenosine diphosphoribose polymerase binding nitroso aromatic compounds useful as retroviral inactivating

agents, anti-retroviral agents and anti-tumor agents-54; Ernest Kun, et al., 546/141 :IMAGE AVAILABLE:

US PAT NO: 5,473,074 :IMAGE AVAILABLE: L1: 53 of 70

ABSTRACT:
The subject invention provides for novel compounds for inactivating viruses. These compounds include 6-nitroso-1,2-benzopyrone, 3-nitrosobenzamide, 5-nitroso-1(2H)-isoquinolinone, 7-nitroso-1(2H)-isoquinolinone, 8-nitroso-1(2H)-isoquinolinone. The invention also provides for compositions containing one or more of the compounds, and for methods of treating viral infections, cancer, infectious virus concentration with the subject compounds and compositions.

54. 5,468,624, Nov. 21, 1995, Cell lysis activity of a modified fragment of the glucocorticoid receptor; E. Brad Thompson, et al., 435/69.1, 69.4, 252.3, 320.1, 372.3; 536/23.5 :IMAGE AVAILABLE:

US PAT NO: 5,468,624 :IMAGE AVAILABLE: L1: 54 of 70

ABSTRACT:
A cell lysis factor which is a modified fragment of the human glucocorticoid receptor. The modified fragment designated 398-465*, when transfected into and expressed in a host cell, effects cell lysis and cell death. A pharmaceutical composition having the modified fragment 398-465* or the encoded protein product may be used in treatment of proliferative diseases.

55. 5,464,871, Nov. 7, 1995, Aromatic nitro and nitroso compounds and their metabolites useful as anti-viral and anti-tumor agents; Ernest Kun, et al., 514/617; 564/166 :IMAGE AVAILABLE:

US PAT NO: 5,464,871 :IMAGE AVAILABLE: L1: 55 of 70

ABSTRACT:
Unsubstituted or substituted halo nitro and nitroso compounds and their metabolites are potent, selective and non-toxic inhibitors and supressants of cancer growth and viral infections in a mammalian host. The compounds are particularly useful for treatment and supression of tumors and viruses associated with breast cancer, AIDS, herpetic episodes and cytomegaloviral infections. The methods of treatment of tumorigenic and viral diseases by halo nitro nitroso compounds and their metabolites are described.

56. 5,462,852, Oct. 31, 1995, HIV Nucleocapsid protein capture assay and method of use; Larry O. Arthur, et al., 435/5, 7.1, 7.92, 7.93, 7.94, 7.95, 971, 974; 436/528, 531, 536, 543; 530/388.1, 388.3, 388.35, 389.4 :IMAGE AVAILABLE:

US PAT NO: 5,462,852 :IMAGE AVAILABLE: L1: 56 of 70

ABSTRACT:
An antigen capture method, and an antigen capture assay diagnostic kit, for detecting the presence or concentration of HIV in a biological sample without interference from antigen-antibody immune complexes is provided. The lysate of a biological sample obtained from an animal is contacted with a detectable amount of an antibody specifically reactive with the nucleocapsid p7 antigen or an immunoreactive fragment of the p7 antigen for a time and under conditions sufficient for p7 antigen contained in the lysate to form a p7-antibody complex. The presence or concentration of this p7-antibody complex is determined to detect or quantitate the presence of HIV in the biological sample. Uses of this assay and method include detecting the presence of HIV infection in an infant born to an HIV-infected mother, monitoring the progression of HIV infection, and evaluating the effectiveness of an anti-HIV treatment administered to an animal, such as a human. Purified antibodies specifically reactive with

an immunoreactive epitope specific to p7 or an immunoreactive fragment of p7 are also provided as well as an antigen capture method for detecting the presence of a lentivirus in a biological sample involving the nucleocapsid protein of the lentivirus.

57. 5,440,017, Aug. 8, 1995, T-cell lymphoma cDNA clones; Carol L. MacLeod, 530/350; 435/69.1, 69.3; 536/23.1; 935/11, 12 :IMAGE AVAILABLE:

US PAT NO: 5,440,017 :IMAGE AVAILABLE: L1: 57 of 70

ABSTRACT:
The present invention provides novel DNA sequences, recombinant DNA (rDNA) molecules, processes for producing novel T-cell proteins expressed in T-cell development, the novel T-cell proteins in substantially pure form and antibodies which bind to the novel proteins. More particularly, it relates to novel DNA sequences expressed in appropriate hosts and the novel T-cell proteins produced in these hosts. The present invention also provides novel transmembrane proteins in substantially pure form, rDNA molecules encoding transmembrane proteins and processes for producing the novel transmembrane proteins. The DNA sequences and recombinant DNA molecules of this invention are characterized in that they are expressed by T lymphoma cells and have at least one of the following characteristics: (1) is expressed in normal thymus, activated spleen cells, or gut associated lymphoid tissue, (2) is expressed in ovarian tissue, normal liver and/or in a stage specific manner in embryonic development and (3) encode novel transmembrane proteins having multiple membrane spanning domains.

58. 5,432,018, Jul. 11, 1995, Peptide library and screening systems; William J. Dower, et al., 435/5, 69.1, 172.3, 235.1; 935/80, 81 :IMAGE AVAILABLE:

US PAT NO: 5,432,018 :IMAGE AVAILABLE: L1: 58 of 70

ABSTRACT:
Peptides which bind to selected receptors are identified by screening libraries which encode a random or controlled collection of amino acids. Peptides encoded by the libraries are expressed as fusion proteins of bacteriophage coat proteins, and bacteriophage are then screened against the receptors of interest. Peptides having a wide variety of uses, such as therapeutic or diagnostic reagents, may thus be identified without any prior information on the structure of the expected ligand or receptor.

59. 5,403,484, Apr. 4, 1995, Viruses expressing chimeric binding proteins; Robert C. Ladner, et al., 435/235.1, 69.7, 172.3, 252.3, 320.1; 530/350; 536/23.4 :IMAGE AVAILABLE:

US PAT NO: 5,403,484 :IMAGE AVAILABLE: L1: 59 of 70

ABSTRACT:
In order to obtain a novel binding protein against a chosen target, DNA molecules, each encoding a protein comprising one of a family of similar potential binding domains and a structural signal calling for the display of the protein on the outer surface of a chosen bacterial cell, bacterial spore or phage (genetic package) are introduced into a genetic package. The protein is expressed and the potential binding domain is displayed on the outer surface of the package. The cells or viruses bearing the binding domains which recognize the target molecule are isolated and amplified. The successful binding domains are then characterized. One or more of these successful binding domains is used as a model for the design of a new family of potential binding domains, and the process is repeated until a novel binding domain having a desired affinity for the target molecule is obtained. In one embodiment, the first family of potential binding domains is related to bovine pancreatic trypsin inhibitor, the genetic package is M13 phage, and the protein includes the outer surface transport signal of the M13 gene III protein.

60. 5,360,893, Nov. 1, 994, DNA sequences encoding pr ns used to elicit and detect programmed cell death; Gregory P. Owens, et al., 530/350 :IMAGE AVAILABLE:

US PAT NO: 5,360,893 :IMAGE AVAILABLE: L1: 60 of 70

ABSTRACT:
Polypeptides and mutants and variants associated with programmed cell death in mammalian cells and DNA sequences, and fragments and derivatives thereof, encoding the polypeptides are disclosed. Also disclosed are methods for detecting programmed cell death in mammalian cells, a method of activating programmed cell death in unwanted mammalian cells, and methods for preventing unwanted cell death occurring in degenerative disorders of mammals.

61. 5,350,840, Sep. 27, 1994, Localization and characterization of the Wilms' tumor gene; Katherine M. Call, et al., 536/23.1; 435/6; 536/24.31; 935/77, 78 :IMAGE AVAILABLE:

US PAT NO: 5,350,840 :IMAGE AVAILABLE: L1: 61 of 70

ABSTRACT:
The Wilms' tumor gene associated with the 11p13 locus on the human chromosome, as well as a method of analyzing cells for the gene is described and characterized. The gene encodes a transcription unit approximately 50 kb in size and a mRNA of approximately 3 kb, which is expressed in a limited number of cell types (e.g., predominantly kidney cells and ja subset of hematopoietic cells). The polypeptide encoded by the Wilms' tumor DNA includes four "**zinc fingers**" and a region rich in proline and glutamine, suggesting that the polypeptide has a role in transcription regulation.

62. 5,338,665, Aug. 16, 1994, Peptide library and screening method; Peter J. Schatz, et al., 435/6, 7.32, 7.37, 172.3, 252.3, 252.33, 320.1; 935/73, 79, 80 :IMAGE AVAILABLE:

US PAT NO: 5,338,665 :IMAGE AVAILABLE: L1: 62 of 70

ABSTRACT:
A random peptide library constructed by transforming host cells with a collection of recombinant vectors that encode a fusion protein comprised of a DNA binding protein and a random peptide and also contain a binding site for the DNA binding protein can be used to screen for novel ligands. The screening method results in the formation of a complex comprising the fusion protein bound to a receptor through the random peptide ligand and to the recombinant DNA vector through the DNA binding protein.

63. 5,312,733, May 17, 1994, Developmental marker gene of CD4-CD8 thymocytes; Carol L. MacLeod, 435/69.1, 71.1, 172.3, 320.1; 530/350; 536/23.1, 23.5; 935/11, 22 :IMAGE AVAILABLE:

US PAT NO: 5,312,733 :IMAGE AVAILABLE: L1: 63 of 70

ABSTRACT:
The present invention provides novel DNA sequences, recombinant DNA (rDNA) molecules, processes for producing novel T-cell proteins expressed in T-cell development, the novel T-cell proteins in substantially pure form and antibodies which bind to the novel proteins. More particularly, it relates to novel DNA sequences expressed in appropriate hosts and the novel T-cell proteins produced in these hosts. The present invention also provides novel transmembrane proteins in substantially pure form, rDNA molecules encoding transmembrane proteins and processes for producing the novel transmembrane proteins. The DNA sequences and recombinant DNA molecules of this invention are characterized in that they are expressed by T lymphoma cells and have at least one of the following

characteristics: (1) is expressed in normal thymus, activated spleen cells, or gut associated lymphoid tissue, (2) is expressed in ovarian tissue, normal liver and/or in a stage specific manner in embryonic development and (3) encode novel transmembrane proteins having multiple membrane spanning domains.

64. 5,270,170, Dec. 14, 1993, Peptide library and screening method; Peter J. Schatz, et al., 435/7.37, 252.33, 320.1; 935/11 :IMAGE AVAILABLE:

US PAT NO: 5,270,170 :IMAGE AVAILABLE: L1: 64 of 70

ABSTRACT:
A random peptide library constructed by transforming host cells with a collection of recombinant vectors that encode a fusion protein comprised of a DNA binding protein and a random peptide and also encode a binding site for the DNA binding protein can be used to screen for novel ligands. The screening method results in the formation of a complex comprising the fusion protein bound to a receptor through the random peptide ligand and to the recombinant DNA vector through the DNA binding protein.

65. 5,262,564, Nov. 16, 1993, Sulfinic acid adducts of organo nitroso compounds useful as retroviral inactivating agents anti-retroviral agents and anti-tumor agents; Ernest Kun, et al., 562/430; 564/98, 99 :IMAGE AVAILABLE:

US PAT NO: 5,262,564 :IMAGE AVAILABLE: L1: 65 of 70

ABSTRACT:
The subject invention provides for novel anti-tumor and anti-retroviral compounds. More specifically, the invention relates to the sulfinic acid adducts of therapeutic C-nitroso compounds. The formation of the adducts increases the stability and more solubility of the C-nitroso compounds. These compounds include the L-cysteinesulfinic acid adducts of 6-nitroso-1,2-benzopyrone and 3-nitrosobenzamide. The invention also provides for compositions containing one or more of the compounds, and for methods of treating retroviral infections, cancer, infectious virus concentration with the subject compounds and compositions.

66. 5,243,041, Sep. 7, 1993, DNA vector with isolated CDNA gene encoding metallopanstimulin; Jose A. Fernandez-Pol, 536/23.5, 24.31 :IMAGE AVAILABLE:

US PAT NO: 5,243,041 :IMAGE AVAILABLE: L1: 66 of 70

ABSTRACT:
A novel DNA sequence is disclosed which encodes a protein associated with many human cancers. This protein is designated as metallopanstimulin-1 (MPS-1) since (1) it is associated with metal ions, particularly zinc; (2) it has been detected in numerous different types of cells; (3) it is associated with rapid cell proliferation. The MPS-1 mRNA and its encoded protein are expressed in normal cells to a much lesser degree than in premalignant or malignant tumor cells, and they are present at very low levels in senescent cells compared to young healthy cells. The DNA sequence and the protein can be used in diagnostic methods such as detection of malignant cells associated with several types of tumors. Thus, this invention discloses a method for determining the presence of certain types of malignant conditions in patients. The MPS-1 cDNA sequence has been inserted into convenient vectors, and a culture of E. coli cells containing the sequence has been deposited with the American Type Culture Collection (ATCC), under accession number ATCC 68656.

67. 5,223,409, Jun. 29, 1993, Directed evolution of novel binding proteins; Robert C. Ladner, et al., 435/69.7, 5, 69.1, 172.3, 252.3, 320.1; 530/387.3, 387.5 :IMAGE AVAILABLE:

US PAT NO: 5,223,4[redacted] IMAGE AVAILABLE: L[redacted] 67 of 70

ABSTRACT:
In order to obtain a novel binding protein against a chosen target, DNA molecules, each encoding a protein comprising one of a family of similar potential binding domains and a structural signal calling for the display of the protein on the outer surface of a chosen bacterial cell, bacterial spore or phage (genetic package) are introduced into a genetic package. The protein is expressed and the potential binding domain is displayed on the outer surface of the package. The cells or viruses bearing the binding domains which recognize the target molecule are isolated and amplified. The successful binding domains are then characterized. One or more of these successful binding domains is used as a model for the design of a new family of potential binding domains, and the process is repeated until a novel binding domain having a desired affinity for the target molecule is obtained. In one embodiment, the first family of potential binding domains is related to bovine pancreatic trypsin inhibitor, the genetic package is M13 phage, and the protein includes the outer surface transport signal of the M13 gene III protein.

68. 5,206,152, Apr. 27, 1993, Cloning and expression of early growth regulatory protein genes; Vikas P. Sukhatme, 435/69.1, 172.3, 235.1, 252.3, 254.11, 320.1; 530/350, 387.9; 536/23.4, 23.5; 935/18, 27, 31, 48, 56, 58, 62, 70, 73, 81 :IMAGE AVAILABLE:

US PAT NO: 5,206,152 :IMAGE AVAILABLE: L1: 68 of 70

ABSTRACT:
Disclosed are DNA sequences encoding novel DNA binding proteins implicated in regulation of early stages of cell growth. Illustratively provided are human and mouse origin DNA sequences encoding early growth regulatory ("Egr") proteins which include "zinc finger" regions of the type involved in DNA binding. Also disclosed are immunological methods and materials for detection of Egr proteins and hybridization methods and materials for detection and quantification of Egr protein related nucleic acids.

69. 5,198,346, Mar. 30, 1993, Generation and selection of novel DNA-binding proteins and polypeptides; Robert C. Ladner, et al., 435/69.1, 172.3, 252.3, 320.1 :IMAGE AVAILABLE:

US PAT NO: 5,198,346 :IMAGE AVAILABLE: L1: 69 of 70

ABSTRACT:
Novel DNA-binding proteins, especially repressors of gene expression, are obtained by variegation of genes encoding known binding proteins and selection for proteins binding the desired target DNA sequence. A novel selection vector may be used to reduce artifacts. Heterooligomeric proteins which bind to a target DNA sequence which need not be palindromic are obtained by a variety of methods, e.g., variegation to obtain proteins binding symmetrized forms of the half-targets and heterodimerization to obtain a protein binding the entire asymmetric target.

70. 5,096,815, Mar. 17, 1992, Generation and selection of novel DNA-binding proteins and polypeptides; Robert C. Ladner, et al., 435/69.1, 172.3, 252.3, 320.1 :IMAGE AVAILABLE:

US PAT NO: 5,096,815 :IMAGE AVAILABLE: L1: 70 of 70

ABSTRACT:
Novel DNA-binding proteins, especially repressors of gene expression, are obtained by variegation of genes encoding known binding protein and selection for proteins binding the desired target DNA sequence. A novel selection vector is used to reduce artifacts. Heterooligimeric proteins which bind to a target DNA sequence which need not be palindromic are

obtained by a variety of methods, e.g., variegation to obtain proteins binding symmetrized forms of the half-targets and heterodimerization to obtain a protein binding the entire asymmetric target.

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L2 3 ZIF268

=> d l2,cit,ab,1-3

1. 5,654,137, Aug. 5, 1997, Human CRABP-I and CRABP-II; Anders Astrom, et al., 435/5, 6, 371 :IMAGE AVAILABLE:

US PAT NO: 5,654,137 :IMAGE AVAILABLE: L2: 1 of 3

ABSTRACT:
The sequences encoding two isoforms of human cellular retinoid acid binding proteins, CRABP-I and CRABP-II, have been cloned and sequenced and are set forth with their corresponding amino acid sequences. The identification of human CRABP nucleic and amino acid sequences provides the basis for the construction of recombinant human CRABP vectors and expression constructs. Human CRABP can also be synthesized or produced ex vivo, e.g. in bacterial or other production systems. Ligand binding assays, including recombinant and chimeric receptor reporter assays, and direct and competition hybridization assays employing the human CRABP sequences herein described can be used to test drugs for retinoid induction and tissue specificity for pathologies in which retinoids are implicated. Immunoassays utilizing antibodies or binding fragments produced to human CRABP can also be used to test patient tissues for the presence and levels of CRABP for diagnosis and to monitor treatment. The identification of the nucleic and amino acids sequences for human CRABP-I and CRABP-II also contributes to the elucidation of the function and interaction of the retinoid-binding proteins.

2. 5,627,024, May 6, 1997, Lambdoid bacteriophage vectors for expression and display of foreign proteins; Ichiro Maruyama, et al., 435/5, 6, 172.3, 320.1; 536/23.4 :IMAGE AVAILABLE:

US PAT NO: 5,627,024 :IMAGE AVAILABLE: L2: 2 of 3

ABSTRACT:
Lambdoid phage comprising a matrix of proteins encapsulating a genome encoding first and second polypeptides of an autogenously assembling receptor and a receptor comprised of the first and second polypeptides surface-integrated into the matrix via a lambdoid phage tail protein matrix anchor domain fused to at least one of the polypeptides.

3. 5,534,542, Jul. 9, 1996, Methods and materials relating to a bi-metallic cross-linking species; Thomas V. O'Halloran, et al., 514/492, 6, 496, 501; 556/28, 136, 137 :IMAGE AVAILABLE:

US PAT NO: 5,534,542 :IMAGE AVAILABLE: L2: 3 of 3

ABSTRACT:
Disclosed herein is a bi-metallic cross-linking reagent according to the following formula: ##STR1## where M.sub.1 is a metal ion species capable of forming a complex of coordination number four or coordination number six; wherein L.sub.1, L.sub.2, L.sub.3, and L.sub.4 are each independently a halide, ammonia, dimethyl sulfoxide, carboxylate, thiolate, imidazole, a nucleobase, or an empty coordination site, provided that no more than two of L.sub.1, L.sub.2, L.sub.3, and L.sub.4 are empty coordination sites; wherein M.sub.2 is a metal ion species capable of forming a complex of coordination number two with a first ligand that is a hydrocarbon moiety and a second ligand that is kinetically lablie; and wherein n is an integer from two to nine. Also disclosed are cross-linked species, methods of preparing the crosslinking reagents of the invention, and methods for their use in tissue-specific